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NEWS 3	APR 15	WPIDS, WPINDEX, and WPIX enhanced with new predefined hit display formats
NEWS 4	APR 28	EMBASE Controlled Term thesaurus enhanced
NEWS 5	APR 28	IMSRESEARCH reloaded with enhancements
NEWS 6	MAY 30	INPAFAMDB now available on STN for patent family searching
NEWS 7	MAY 30	DGENE, PCTGEN, and USGENE enhanced with new homology sequence search option
NEWS 8	JUN 06	EPFULL enhanced with 260,000 English abstracts
NEWS 9	JUN 06	KOREAPAT updated with 41,000 documents
NEWS 10	JUN 13	USPATFULL and USPAT2 updated with 11-character patent numbers for U.S. applications
NEWS 11	JUN 19	CAS REGISTRY includes selected substances from web-based collections
NEWS 12	JUN 25	CA/CAplus and USPAT databases updated with IPC reclassification data
NEWS 13	JUN 30	AEROSPACE enhanced with more than 1 million U.S. patent records
NEWS 14	JUN 30	EMBASE, EMBAL, and LEMBASE updated with additional options to display authors and affiliated organizations
NEWS 15	JUN 30	STN on the Web enhanced with new STN AnaVist Assistant and BLAST plug-in
NEWS 16	JUN 30	STN AnaVist enhanced with database content from EPFULL
NEWS 17	JUL 28	CA/CAplus patent coverage enhanced
NEWS 18	JUL 28	EPFULL enhanced with additional legal status information from the epoline Register
NEWS 19	JUL 28	IFICDB, IFIPAT, and IFIUDB reloaded with enhancements
NEWS 20	JUL 28	STN Viewer performance improved
NEWS 21	AUG 01	INPADOCDB and INPAFAMDB coverage enhanced
NEWS 22	AUG 13	CA/CAplus enhanced with printed Chemical Abstracts page images from 1967-1998
NEWS 23	AUG 15	CAOLD to be discontinued on December 31, 2008
NEWS 24	AUG 15	CAplus currency for Korean patents enhanced
NEWS 25	AUG 25	CA/CAplus, CASREACT, and IFI and USPAT databases enhanced for more flexible patent number searching
NEWS 26	AUG 27	CAS definition of basic patents expanded to ensure comprehensive access to substance and sequence information
NEWS 27	SEP 18	Support for STN Express, Versions 6.01 and earlier, to be discontinued
NEWS 28	SEP 25	CA/CAplus current-awareness alert options enhanced

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                  to accommodate supplemental CAS indexing of
                  exemplified prophetic substances
 NEWS 29  SEP 26  WPIDS, WPINDEX, and WPIX coverage of Chinese and
                  and Korean patents enhanced
 NEWS 30  SEP 29  IFICLS enhanced with new super search field
 NEWS 31  SEP 29  EMBASE and EMBAL enhanced with new search and
                  display fields
 NEWS 32  SEP 30  CAS patent coverage enhanced to include exemplified
                  prophetic substances identified in new Japanese-
                  language patents

 NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
              AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

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                                                         ENTRY    SESSION
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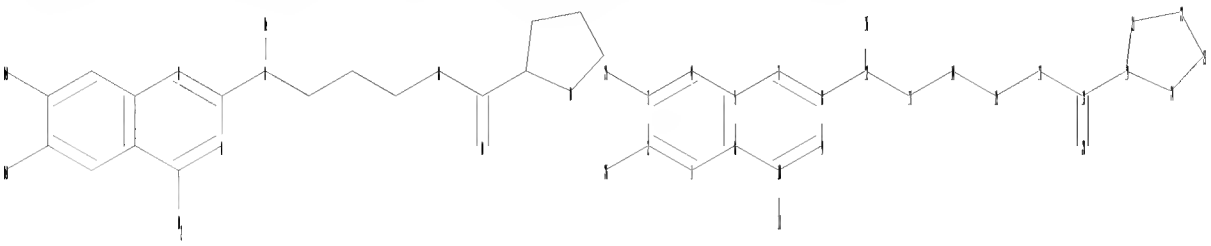
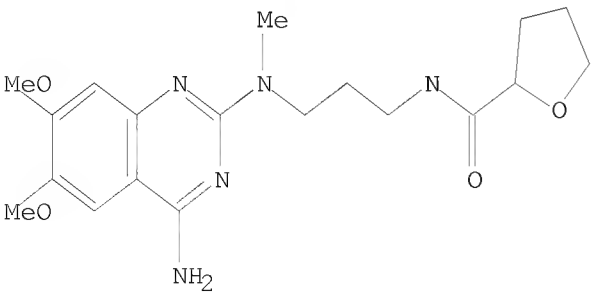


chain nodes :
11 12 13 14 15 16 17 18 20 25 26
ring nodes :
1 2 3 4 5 6 7 8 9 10 19 21 22 23 24
chain bonds :
2-26 3-25 8-12 10-11 12-13 12-16 13-14 14-15 15-17 17-18 18-19 18-20
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10 19-21 19-24 21-22 22-23
23-24
exact/norm bonds :
8-12 10-11 12-13 15-17 17-18 18-20
exact bonds :
2-26 3-25 12-16 13-14 14-15 18-19 19-21 19-24 21-22 22-23 23-24
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10
isolated ring systems :
containing 1 : 19 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS
19:Atom 20:CLASS 21:Atom 22:Atom 23:Atom 24:Atom 25:CLASS 26:CLASS

L1 STRUCTURE UPLOADED

=> d L1
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

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=> s l1
SAMPLE SEARCH INITIATED 10:56:18 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -        7 TO ITERATE

100.0% PROCESSED        7 ITERATIONS                                 6 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            7 TO      298
PROJECTED ANSWERS:               6 TO      266

L2            6 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 10:56:29 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      126 TO ITERATE

100.0% PROCESSED      126 ITERATIONS                                86 ANSWERS
SEARCH TIME: 00.00.01

L3           86 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   178.82     179.03

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FILE LAST UPDATED: 5 Oct 2008  (20081005/ED)

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http://www.cas.org/legal/infopolicy.html

=> s l3
L4          360 L3

=> s l4 not py>2003
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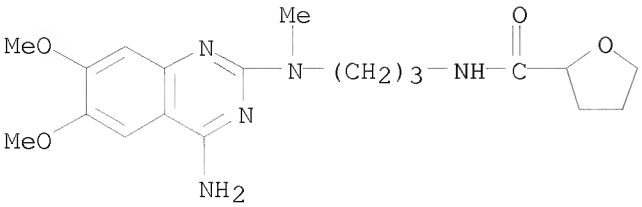
6322349 PY>2003
L5 127 L4 NOT PY>2003

=> d l5 1- ibib abs hitstr
YOU HAVE REQUESTED DATA FROM 127 ANSWERS - CONTINUE? Y/(N):y

L5 ANSWER 1 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:38531 CAPLUS
DOCUMENT NUMBER: 140:104900
TITLE: Use of α-blockers and the risk of hip/femur fractures
AUTHOR(S): Souverein, P. C.; Van Staa, T. P.; Egberts, A. C. G.; De La Rosette, J. J. M. C. H.; Cooper, C.; Leufkens, H. G. M.
CORPORATE SOURCE: Department of Pharmacoepidemiology and Pharmacotherapy, Utrecht Institute for Pharmaceutical Sciences, Utrecht, Neth.
SOURCE: Journal of Internal Medicine (2003), 254(6), 548-554
CODEN: JINMEO; ISSN: 0954-6820
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Objective: To study the association between use of α-blockers and risk of hip/femur fractures. Design: Population-based case-control study. Setting: General Practice Research Database. Subjects: Cases were defined as men, aged 40 yr and older with a first diagnosis for hip/femur fracture. Controls were matched 1: 1 on gender, year of birth and general practitioner-practice. Results: In all, 4571 cases and an equal number of controls were identified. Current use of α-blockers (prazosin, doxazosin, indoramin, terazosin, alfuzosin and tamsulosin) was compared with non-use of α-blockers. Current use of α-blockers on the index date was associated with an increased risk of hip/femur fracture [adjusted odds ratio (OR) 1.9, 95% confidence interval (CI): 1.1-3.0] in the overall anal. The effect was particularly strong for first prescriptions within a treatment episode (adjusted OR 5.1, 95% CI: 1.0-31.7) and during the first month of treatment (adjusted OR 4.1, 95% CI: 0.7-23.9). Stratification according to indication of use showed that current use of α-blockers was not associated with hip/femur fracture in men with a diagnosis of benign prostatic hyperplasia (adjusted OR 1.0, 95% CI: 0.4-2.5), but was associated in men who used α-blockers for cardiovascular disease (adjusted OR 2.8, 95% CI: 1.4-5.4). Conclusion: Current use of α-blockers was associated with an increased risk of hip/femur fracture and with the start of a new treatment episode. The effect seemed to be confined to patients who used α-blockers for cardiovascular disease. Caution with respect to first-dose effects related to the initiation of a new episode of α-blocker treatment is advised.
IT 81403-80-7, Alfuzosin
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α-blockers and the risk of hip and femur fractures)
RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



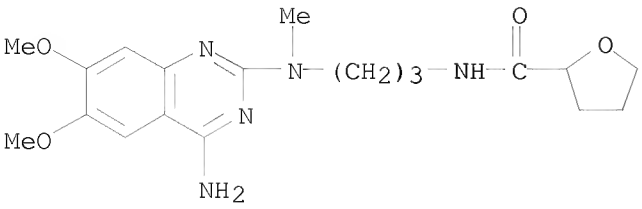
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:851019 CAPLUS
DOCUMENT NUMBER: 140:399006
TITLE: Alfuzosin for the management of benign prostate hyperplasia
AUTHOR(S): Weiner, David M.; Lowe, Franklin C.
CORPORATE SOURCE: Columbia University College of Physicians and Surgeons, New York, NY, 10019, USA
SOURCE: Expert Opinion on Pharmacotherapy (2003), 4(11), 2057-2063
CODEN: EOPHF7; ISSN: 1465-6566
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Alfuzosin (UroXatral, Sanofi-Synthelabo) a quinazoline derivative, has well-documented α1-adrenoreceptor antagonist activity. These receptors are present in the smooth muscle located at the bladder base, proximal urethra, prostate and prostatic capsule as well as in vascular and nervous systems. Consequently, alfuzosin has the ability to reduce the tone of these areas, effectively decreasing bladder outlet resistance. A sustained-release formulation of alfuzosin is currently available in Europe and is FDA-approved in the US. The confirmed efficacy, proven bioavailability and good cardiovascular safety profile support the use of this drug for the management of lower urinary tract symptoms secondary to benign prostate hyperplasia (BPH). These findings have been confirmed in a large cohort of patients treated in general practice. Addnl., treatment with alfuzosin has demonstrated a favorable impact on quality of life of patients with BPH.

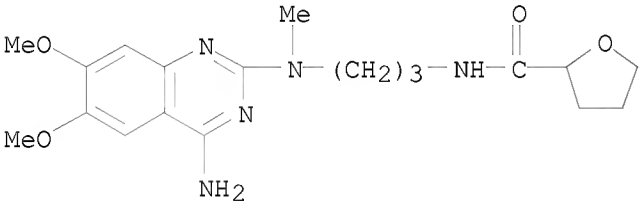
IT 81403-68-1, UroXatral 81403-80-7, Alfuzosin
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of alfuzosin α1-adrenergic receptor blocker in treating lower urinary tract symptom (LUTS) secondary to benign prostate hyperplasia in humans and uroselective, minimal side effects, minimal drug interaction)

RN 81403-68-1 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

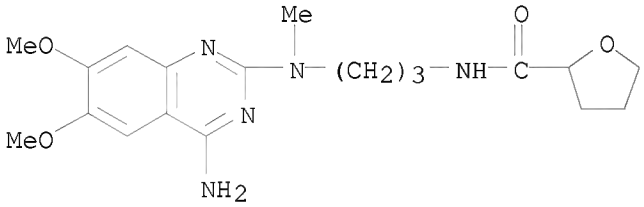
L5 ANSWER 3 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:786742 CAPLUS
DOCUMENT NUMBER: 140:192967
TITLE: Role of the impairment of oxidative metabolism in pathogenesis of lower urinary tract symptoms with benign prostatic hyperplasia and their treatment by α1-adrenoblocker alfuzosin
AUTHOR(S): Vishnevsky, E. L.; Kondrashova, M. N.; Pushkar, D. Y.; Vishnevsky, E.; Demidov, A. A.; Sirota, T. V.; Temnov, A. V.; Khunderyakova, N. V.; Zakharchenko, M. V.; Kosyakova, N. I.
CORPORATE SOURCE: Department of Urology, Moscow Medical University, Moscow, Russia
SOURCE: Mitochondrion (2003), 3(2), 67-73
CODEN: MITOCN; ISSN: 1567-7249
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The role of impairment of general oxidative and energy metabolism in pathogenesis of lower urinary tract symptoms (LUTS) in patients with benign prostatic hyperplasia (BPH) and their correction by (1-adrenoblocker alfuzosin was studied). One group of patients (N=126) was examined by standard methods for determination of the severity of LUTS by IPSS and mean effective volume of urinary bladder (MEVUB). In the second group (N=29) in addition to functional examns., metabolic indicators in blood were measured: antioxidant activity (AOA) and succinate dehydrogenase activity (SDA). Severity of LUTS depends greatly on the MEVUB. It was the first to show a practically complete correlation between LUTS, AOA and SDA.

Severity of LUTS exactly correlates with indicators of oxidative and energy metabolism In patients with more heavy LUTS, lowest AOA and SDA values were found. In the course of effective treatment, both phenomena developed an improvement of clin. symptoms and a rise of biochem. parameters. Close correlation between functional and metabolic phenomena is evidence of an essential role of metabolic mechanisms in the pathogenesis of LUTS with BPH. This opens perspectives to use antioxidants and energy metabolism activators for correction of UB dysfunction in patients with BPH.

IT 81403-80-7, Alfuzosin
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(role of impairment of oxidative metabolism in pathogenesis of lower urinary tract symptoms with benign prostatic hyperplasia and their treatment by α1-adrenoblocker alfuzosin)

RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:734114 CAPLUS

DOCUMENT NUMBER: 139:286224

TITLE: Safety and efficacy of alfuzosin 10 mg once-daily in the treatment of lower urinary tract symptoms and clinical benign prostatic hyperplasia: a pooled analysis of three double-blind, placebo-controlled studies

AUTHOR(S): Roehrborn, C. G.; Van Kerrebroeck, P.; Nordling, J.

CORPORATE SOURCE: Department of Urology, The University of Texas Southwestern Medical Center at Dallas, Dallas, USA

SOURCE: BJU International (2003), 92(3), 257-261
CODEN: BJINFO; ISSN: 1464-4096

PUBLISHER: Blackwell Publishing Ltd.

DOCUMENT TYPE: Journal

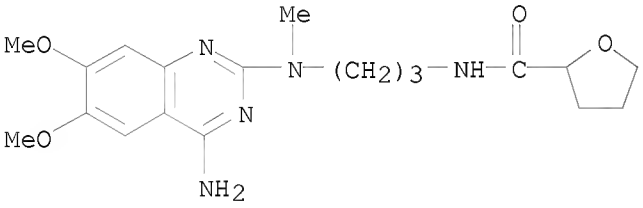
LANGUAGE: English

AB The purpose of this study was to examine the efficacy and safety of a once-daily formulation of alfuzosin in a pooled anal. of three parallel, randomized, double-blind, placebo-controlled 3-mo studies of patients with lower urinary tract symptoms (LUTS) consistent with clin. benign prostatic hyperplasia. Patients were randomized to receive alfuzosin, 10 mg once-daily (473) or placebo (482) for 12 wk. Primary efficacy criteria were improvements in the International Prostate Symptom Score (IPSS) and peak urinary flow rate (PFR). Alfuzosin significantly improved the mean (SD) IPSS, by -6.0 (5.1) vs -4.2 (5.7) with placebo ($P < 0.005$) and the PFR, by +2.3 (3.8) vs +1.1 (3.1) ml/s with placebo ($P < 0.001$), irresp. of prostate size. The significant improvement in LUTS included the irritative and the obstructive subscore of the IPSS and the nocturia

criterion; the PFR increased rapidly and significantly, from the first visit (14 days). The quality-of-life score also improved significantly in alfuzosin-treated patients. Alfuzosin was well tolerated; the number of withdrawals for adverse events was comparable in both treatment groups. The most frequently reported adverse event was dizziness (placebo 2.9%, alfuzosin 6.1%). There were no significant changes in blood pressure with alfuzosin compared with placebo, including in elderly and hypertensive patients. Sexual adverse events were rare (abnormal ejaculation, 0.6%). CONCLUSIONS The once-daily formulation of alfuzosin, administered at 10 mg with no dose titration is effective, with a good safety profile, especially in elderly and hypertensive patients.

IT 81403-80-7, Alfuzosin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(safety and efficacy of alfuzosin treatment of lower urinary tract symptoms and clin. benign prostatic hyperplasia)

RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)

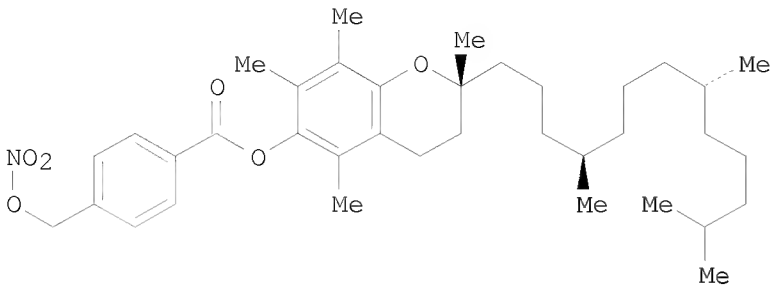


REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:652131 CAPLUS
DOCUMENT NUMBER: 139:214237
TITLE: Preparation of nitrate prodrugs able to release nitric oxide in a controlled and selective way and their use for prevention and treatment of inflammatory, ischemic and proliferative diseases
INVENTOR(S): Scaramuzzino, Giovanni
PATENT ASSIGNEE(S): Italy
SOURCE: Eur. Pat. Appl., 313 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1336602	A1	20030820	EP 2002-425075	20020213
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRIORITY APPLN. INFO.:			EP 2002-425075	20020213

GI



II

AB New pharmaceutical compds. of general formula F-(X)q (I) [q = 1-5, preferably 1; F is chosen among drugs such as δ-tocopherol, clidanac, diethylhomospermine, glucosamine, thymocartin, vofopitant, etc.; X is chosen among 4 groups M, T, V, and Y where M = ONO2, nitrate salt, nitrite ester, ONO, thoinitrite, SNO, etc., T = OR1-M, OR1OR1-M, SR1NR2R1-M, NR2R1-M, NR2R1SR1-M, etc., R1 = saturated or unsatd., linear or branched alkylene, having 1 to 21 carbon atoms or a saturated or unsatd., optionally heterosubstituted or branched cycloalkylene, having 3 to 7 carbon atoms or an optionally heterosubstituted arylene having 3 to 7 carbon atoms; R2 = H, saturated or unsatd., linear or branched 1-21 carbon atom alkyl, saturated or unsatd. optionally heterosubstituted or branched 3-7 carbon cycloalkyl, optionally heterosubstituted 3-7 carbon aryl; R1, R2 = OH, SH, F, Cl, Br, OPO3H2, CO2H, etc.; bond between F and T = carboxylic ester, carboxylic amide, glycoside, azo, thioester, sulfonic ester, etc.; V = Z-M2, OZ-M2, NR2Z-M2, R1Z-M2, OR1-M2, OR1Z-M2, M2 = M, R1-M, OR1-M, SR1-M, NR2R1-M; ZM2 = COCH2CH(M2)CH2N+Me3, COCH2CH2COM2, COCH(NHR2)CH2M2, etc.; Y = 4-COC6H4CH2ONO2, O(CH2)4ONO2, COCH(NH2)CH2ONO2, 3-OC6H4CH2ONO2, etc.] were prepared For example, α-tocopherol reacted with 4-HO2CC6H4CH2ONO2 to give the nitroxymethyl derivative II. The compds. of general formula I are nitrate prodrugs which can release nitric oxide in vivo in a controlled and selective way and without hypotensive side effects and for this reason they are useful for the preparation of medicines for prevention and treatment of inflammatory, ischemic, degenerative and proliferative diseases of musculoskeletal, tegumental, respiratory, gastrointestinal, genito-urinary and central nervous systems.

IT 586349-57-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

RN 586349-57-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro-, nitrate (1:?) (CA INDEX NAME)

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CRN 81403-80-7
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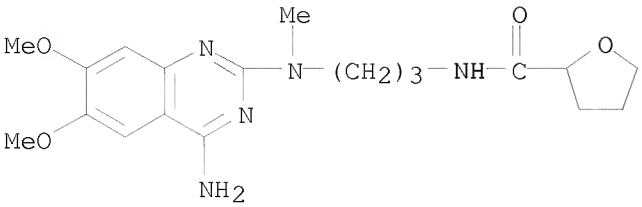
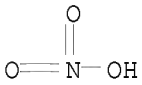


CM 2

CRN 7697-37-2
CMF H N O3



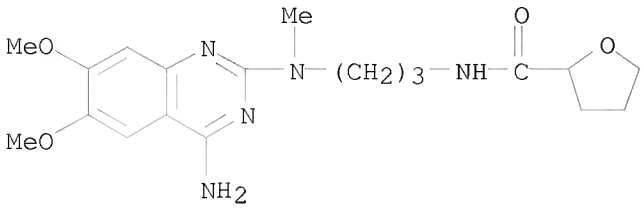
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:621468 CAPLUS
DOCUMENT NUMBER: 139:240306
TITLE: Prostatic tissual distribution of alfuzosin in patients with benign prostatic hyperplasia following repeated oral administration
AUTHOR(S): Mottet, Nicolas; Bressolle, Francoise; Delmas, Vincent; Robert, Michele; Costa, Pierre
CORPORATE SOURCE: Urology Department, Central Hospital Gaston Doumergue, Nimes, 30029/9, Fr.
SOURCE: European Urology (2003), 44(1), 101-105
CODEN: EUURAV; ISSN: 0302-2838
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The blood and prostatic concns. of alfuzosin were determined in patients with benign prostatic hyperplasia (BPH). 12 Patients scheduled for BPH surgery were treated with alfuzosin 5 mg twice daily prior to surgery in an open trial. Seven doses were given over a 4-day period. Blood samples were drawn before the first and the last intake (day 3). On day 4 (surgery day), a blood and prostate tissue sample were taken simultaneously 12 h after the last drug intake. Mean trough blood levels were 6.0 ± 4.6 ng/mL and 5.8 ± 3.7 ng/mL on day 3 and day 4, resp., indicating a stable alfuzosin concentration The mean prostate concentration on day 4 was 12.3 ± 5.6 ng/g. Alfuzosin prostate and blood concns. at 12 h post dosing on day 4 were significantly correlated (r = 0.804, p = 0.0016); the prostate-blood ratio was 2.4 ± 0.7. Oral administration of alfuzosin leads to a high diffusion of the drug into the prostate of BPH patients.

IT 81403-80-7, Alfuzosin
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prostatic tissual distribution of alfuzosin in patients with benign prostatic hyperplasia)

RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



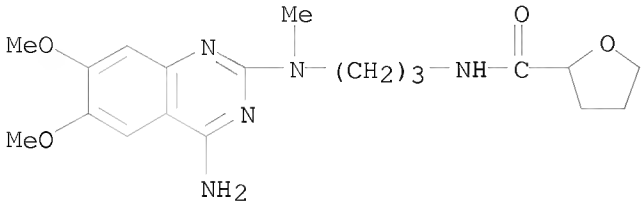
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:621435 CAPLUS
DOCUMENT NUMBER: 139:239478
TITLE: Alfuzosin hydrochloride for the treatment of benign prostatic hyperplasia
AUTHOR(S): Lee, Mary
CORPORATE SOURCE: Chicago College of Pharmacy, Downers Grove, IL, 60515, USA
SOURCE: American Journal of Health-System Pharmacy (2003), 60(14), 1426-1439
CODEN: AHSPEK; ISSN: 1079-2082
PUBLISHER: American Society of Health-System Pharmacists
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. The chemical, pharmacol., pharmacokinetics, clin. efficacy, and adverse effects of alfuzosin hydrochloride in the treatment of benign prostatic hyperplasia (BPH) are discussed. Alfuzosin is a functionally uroselective α1-adrenergic antagonist indicated for the management of moderate to severe BPH. It can improve urinary voiding symptoms and increase urinary flow rates while causing few cardiovascular adverse effects. When administered as an immediate-release (IR) formulation, alfuzosin must be administered twice or thrice daily. The extended-release (ER) formulations of alfuzosin for once- or twice-daily administration are associated with small variations in peak and trough serum drug levels, which may contribute to the lower frequency of cardiovascular adverse effects reported with ER vs. IR alfuzosin. Alfuzosin has been shown to improve patients' perception of quality of life, allowing patients to increase their phys. activities and improve their ability to handle day-to-day activities. Less significant improvements in patients' sense of well-being and improved sexual functioning have been reported. The usual dose of alfuzosin for patients with BPH is 2.5 mg twice or thrice daily of the IR formulation or 5 mg of ER alfuzosin twice daily or 10 mg of ER alfuzosin once daily. The Food and Drug Administration is currently reviewing the ER 10-mg formulation for once-daily administration. IR alfuzosin is similar to all other second-generation α1-adrenergic antagonists in mechanism of action, clin. efficacy, and adverse effects. No dosage titration is needed for ER alfuzosin, and its onset of peak action is within days of the start of treatment.

IT 81403-68-1, Alfuzosin hydrochloride
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alfuzosin hydrochloride for treatment of benign prostatic hyperplasia

patients)
RN 81403-68-1 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

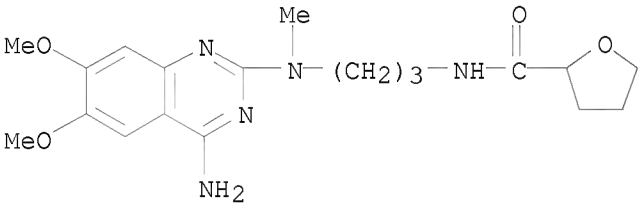
REFERENCE COUNT: 95 THERE ARE 95 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:565169 CAPLUS
DOCUMENT NUMBER: 140:669
TITLE: Comparison of the relaxant effects of alfuzosin, phentolamine and sildenafil on rabbit isolated corpus cavernosum
AUTHOR(S): Palea, S.; Barras, M.
CORPORATE SOURCE: Department of Internal Medicine, Sanofi-Synthelabo Recherche, Rueil-Malmaison, Fr.
SOURCE: BJU International (2003), 91(9), 873-877
CODEN: BJINFO; ISSN: 1464-4096
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB OBJECTIVE: To compare the direct relaxant effects of alfuzosin, phentolamine and sildenafil in rabbit isolated corpus cavernosum (CC) precontracted with phenylephrine or KCl. MATERIALS AND METHODS: Penile erectile tissue was obtained from male New Zealand White rabbits (22-26 wk old). The CC was cut into longitudinal strips and mounted under 2 g resting tension in 5-mL jacketed organ baths containing a modified Krebs solution
bubbled with 95% O2, 5% CO2 and maintained at 37°. Tissue strips were precontracted by 60 mmol/L KCl or 10 μmol/L phenylephrine. After obtaining a stable plateau of contractions, test compds. were added to the organ bath. The relaxant potencies were expressed as the percentage of inhibition of the plateau of contraction induced by 10 μmol/L phenylephrine. RESULTS: Alfuzosin showed a concentration-dependent relaxing effect on rabbit CC precontracted by 10 μmol/L phenylephrine, with a mean pIC50 of 7.64. The relaxant effect was unaffected by preincubation with 100 μmol/L Nω-nitro-L-arginine Me ester (L-NAME). Phentolamine had a potency similar to alfuzosin, with a pIC50 of 7.44. Both alfuzosin and phentolamine were completely ineffective on the plateau of contraction induced by 60 mmol/L KCl. In contrast to alfuzosin, sildenafil was equipotent in relaxing the rabbit CC against each contractile agent, with pIC50 values of 7.25 and 7.23 with 10 μmol/L phenylephrine and 60 mmol/L KCl, resp. The relaxant response to sildenafil was partly blocked by pretreatment with 100 μmol/L L-NAME,

with pIC50 values of 7.94 and 6.63 without and with L-NAME, resp. Sildenafil, incubated for 45 min at 10 μmol/L, had no relaxant effect on the resting tension of the preparation or on the concentration-response curve to phenylephrine. CONCLUSIONS: The direct relaxant effect of alfuzosin is mediated through α-adrenoceptor blockade. The relaxations induced by phentolamine and alfuzosin are independent of nitric oxide, whereas those induced by sildenafil are, at least partly, sensitive to L-NAME and a selective soluble guanylate cyclase inhibitor, indicating the involvement of nitric oxide and soluble guanylate cyclase. Alfuzosin and phentolamine effectively counteract α-adrenoceptor-mediated contractions of rabbit CC. If valid for human CC, such an effect may contribute to an improved erectile function in patients treated for benign prostatic hyperplasia.

IT 81403-80-7, Alfuzosin
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); BIOL (Biological study)
(alfuzosin and phentolamine and sildenafil comparative relaxant effects on rabbit isolated corpus cavernosum and mechanisms thereof)

RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:479403 CAPLUS
DOCUMENT NUMBER: 139:312566
TITLE: Chiral separation and preparation of three new antagonists of α1-adrenoceptors by chiral mobile phase HPLC
AUTHOR(S): Niu, Changqun; Ren, Leiming
CORPORATE SOURCE: Department of Pharmacology, School of Pharmacy, Hebei Medical University, Shijiazhuang, 050017, Peop. Rep. China
SOURCE: Yaoxue Xuebao (2002), 37(6), 450-453
CODEN: YHHPAL; ISSN: 0513-4870
PUBLISHER: Yaoxue Xuebao Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

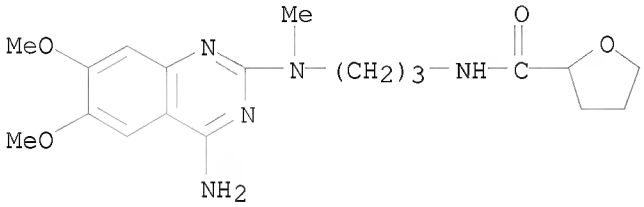
AB The new method for the chiral separation and preparation of three new drugs, alfuzosin, terazosin, and doxazosin was presented. By optimizing factors which affect the chiral separation, modifier of solvent, chiral additive, pH of mobile phase, modifier of organic base and stationary phase, the optimum condition for chiral separation were selected. The preparation of enantiomers was carried out on semi-preparative reverse phase column (7.8 mm x 250 mm C4 5 μm). Acetonitrile-water, modified with carboxymethyl-β-cyclodextrin (2-5%, w/v), was applied as chiral mobile phase. The

enantiomers of three new drugs were baseline-separated and milligram-scale samples of enantiomer were obtained. The method can be used in research and development of the enantiomers of three new drugs.

IT 81403-80-7, Alfuzosin
RL: ANT (Analyte); ANST (Analytical study)
(separation of alfuzosin, terazosin and doxazosin by HPLC)

RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



L5 ANSWER 10 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:294817 CAPLUS

DOCUMENT NUMBER: 139:143240

TITLE: Selective, sensitive and rapid liquid chromatography-tandem mass spectrometry method for the determination of alfuzosin in human plasma

AUTHOR(S): Wiesner, J. L.; Sutherland, F. C. W.; van Essen, G. H.; Hundt, H. K. L.; Swart, K. J.; Hundt, A. F.

CORPORATE SOURCE: FARMOVS-PAREXEL Clinical Research Organisation, Brandhof, 9324, S. Afr.

SOURCE: Journal of Chromatography, B: Analytical Technologies in the Biomedical and Life Sciences (2003), 788(2), 361-368
CODEN: JCBAAI; ISSN: 1570-0232

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

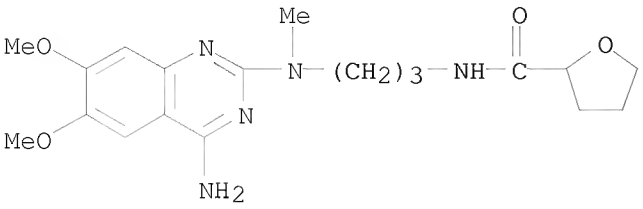
AB A selective, sensitive and rapid liquid chromatog.-tandem mass spectrometry method for the determination of alfuzosin in plasma was developed. A PE Sciex API 2000 triple quadrupole mass spectrometer in multiple reaction monitoring (MRM) mode, using TurboIonSpray with pos. ionization was used. Using prazosin as an internal standard, liquid-liquid extraction was followed by C18 reversed-phase liquid chromatog. and tandem mass spectrometry. The mean recovery for alfuzosin was 82.9% with a lower limit of quantification set at 0.298 ng/mL, the calibration range being between 0.298 and 38.1 ng/mL. This assay method makes use of the increased sensitivity and selectivity of tandem mass spectrometric (MS-MS) detection to allow for a more rapid (extraction and chromatog.) and selective method for the determination of alfuzosin in human plasma than was previously described. The assay method was used to quantify alfuzosin in human plasma samples generated in a multiple-dose (5 mg bd.) study at steady state.

IT 81403-80-7, Alfuzosin
RL: ANT (Analyte); ANST (Analytical study)
(selective, sensitive and rapid liquid chromatog.-tandem mass spectrometry method for the determination of alfuzosin in human plasma)

RN 81403-80-7 CAPLUS

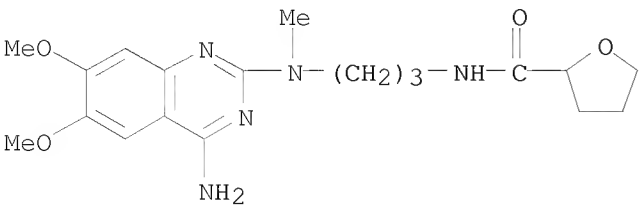
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-

quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 11 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:49279 CAPLUS
DOCUMENT NUMBER: 139:159420
TITLE: Discrimination and selection of new potential antibacterial compounds using simple topological descriptors
AUTHOR(S): Murcia-Soler, Miguel; Perez-Gimenez, Facundo; Garcia-March, Francisco J.; Salabert-Salvador, M. Teresa; Diaz-Villanueva, Wladimiro; Medina-Casamayor, Piedad
CORPORATE SOURCE: Faculty of Pharmacy, Department of Physical Chemistry, Universitat de Valencia, Valencia, Spain
SOURCE: Journal of Molecular Graphics & Modelling (2003), 21(5), 375-390
CODEN: JMGMFI; ISSN: 1093-3263
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The aim of the work was to discriminate between antibacterial and non-antibacterial drugs by topol. methods and to select new potential antibacterial agents from among new structures. The method used for antibacterial activity selection was a linear discriminant anal. (LDA). It is possible to obtain a QSAR interpretation of the information contained in the discriminant function. We make use of the pharmacol. distribution diagrams (PDDs) as a visualizing technique for the identification and selection of new antibacterial agents.
IT 81403-80-7, Alfuzosin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(discrimination and selection of new potential antibacterial compds. using simple topol. descriptors)
RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)

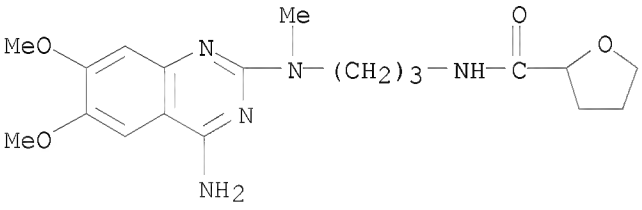


REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 12 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:8976 CAPLUS
DOCUMENT NUMBER: 139:206753
TITLE: Current concepts in the pharmacotherapy of benign prostatic hyperplasia
AUTHOR(S): Khastgir, Jay; Arya, Manit; Shergill, Iqbal S.; Kalsi, Jas S.; Minhas, Sux; Mundy, Anthony R.
CORPORATE SOURCE: Institute of Urology, London, W1W 7EY, UK
SOURCE: Expert Opinion on Pharmacotherapy (2002), 3(12), 1727-1737
CODEN: EOPHF7; ISSN: 1465-6566
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Benign prostatic hyperplasia is a major men's health issue, with .apprx.80% of all men developing this condition within their lifetime. A variety of oral treatments is available, including α-adrenoceptor antagonists (α-blockers), 5α-reductase inhibitors, aromatase inhibitors and phytotherapy. A large number of α-blockers can be administered, but no single agent has demonstrated a clear superiority over the other drugs. 5αReductase inhibitors have demonstrated similar efficacy in larger volume prostates but most evidence suggests that there is no benefit in combining them with α-blockers. The use of phytotherapy is not entirely novel but requires further long-term evaluation before it can be endorsed for clin. use in benign prostatic hyperplasia.

IT 81403-80-7, Alfuzosin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacotherapy of benign prostatic hyperplasia)
RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 109 THERE ARE 109 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

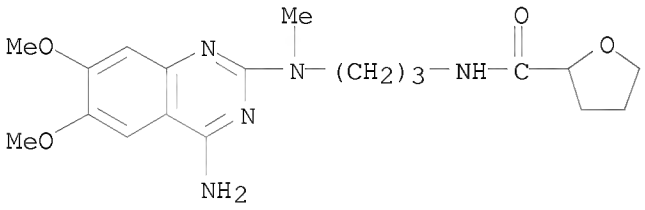
L5 ANSWER 13 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:949951 CAPLUS
DOCUMENT NUMBER: 138:19095
TITLE: Pharmacokinetics and safety of a single oral dose of once-daily alfuzosin, 10 mg, in male subjects with mild to severe renal impairment
AUTHOR(S): Marbury, Thomas C.; Blum, Robert A.; Rauch, Clemence; Pinquier, Jean-Louis
CORPORATE SOURCE: Orlando Clinical Research Center, Orlando, FL, USA

SOURCE: Journal of Clinical Pharmacology (2002), 42(12), 1310-1317
CODEN: JCPCBR; ISSN: 0091-2700
PUBLISHER: Sage Publications
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effect of renal impairment on the safety and pharmacokinetics of a once-daily formulation of alfuzosin, 10 mg, was evaluated. In an open, single-dose study, 26 volunteers, ages 18 to 65 yr, were classified as having normal renal function (n = 8) or mild (n = 6), moderate (n = 6), or severe (n = 6) renal impairment. Mean Cmax values increased by a factor of 2.20, 2.52, and 2.20 in subjects with mild, moderate, or severe renal impairment, resp., compared with controls. Values for AUC0-∞ were 2.46, 1.47, and 1.44, resp. The t1/2z was increased only in the group with severe renal impairment. Emergent vasodilatory adverse events were reported by 4 of 26 subjects. No discontinuations due to adverse events occurred. Laboratory parameters were satisfactory in all groups. In conclusion, once-daily alfuzosin, 10 mg, could be safely administered to patients with impaired renal function, and dosage adjustment does not seem necessary.

IT 81403-80-7, Alfuzosin
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacokinetics and safety of oral once-daily alfuzosin in male subjects with mild to severe renal impairment)

RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 14 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:949490 CAPLUS
DOCUMENT NUMBER: 138:19405

TITLE: Alfuzosin in the treatment of high leak-point pressure in children with neurogenic bladder

AUTHOR(S): Schulte-Baukloh, H.; Michael, T.; Miller, K.; Knispel, H. H.
CORPORATE SOURCE: St. Hedwig Hospital (Teaching Hospital), Free University of Berlin, Berlin, Germany

SOURCE: BJU International (2002), 90(7), 716-720
CODEN: BJINFO; ISSN: 1464-4096
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

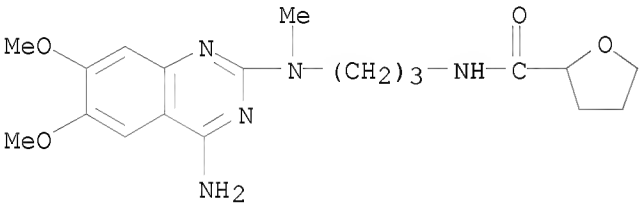
AB Objectives: To decrease the detrusor leak-point pressure (LPP) of > 40 cmH2O in children with a neurogenic bladder, using the α1-adrenergic blocking agent alfuzosin. Patients and methods: Videocystometry was used

to measure the detrusor LPP and several other variables before and 3 wk after the oral administration of alfuzosin (2.5-7.5 mg/day) in 17 children (mean age 6.3 yr) with an upper motor neuron lesion. Results: The mean (SD) detrusor LPP decreased from 68(37) to 46(31) cmH2O (P<0.01), reflex volume (defined as the volume at the first uninhibited bladder contraction of > 15 cmH2O) increased from 78 (69) to 112 (118) mL (+44%), bladder compliance increased from 9.3 (6.1) to 19.6 (14.6) mL/cmH2O (+111%), maximal vesical pressure decreased from 84 (40) to 70 (47) cmH2O (-17%), and the mean number of uninhibited bladder contractions decreased from 6.3 to 3.5 (-44%). The therapy was well tolerated; side-effects were rare and not severe. Intermittent catheterization could be avoided in six children. Conclusion: Alfuzosin decreases the detrusor LPP in children with a neurogenic bladder caused by an upper motor neuron lesion, significantly and therapeutically, and should be considered as an alternative or addition to intermittent catheterization and anticholinergic drugs in selected patients.

IT 81403-80-7, Alfuzosin
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alfuzosin in treatment of high leak-point pressure in children with neurogenic bladder)

RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 15 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:884701 CAPLUS

DOCUMENT NUMBER: 137:362799

TITLE: Randomised, placebo controlled, double blind study of alfuzosin SR in patients undergoing trial without catheter following acute urinary retention

AUTHOR(S): Shah, T.; Palit, V.; Biyani, S.; Elmasry, Y.; Puri, R.; Flannigan, G. M.

CORPORATE SOURCE: Department of Urology, Bradford Hospitals NHS Trust, St. Lukes Hospital, Bradford, West Yorkshire, BD5 0NA, UK

SOURCE: European Urology (2002), 42(4), 329-332
CODEN: EUURAV; ISSN: 0302-2838

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

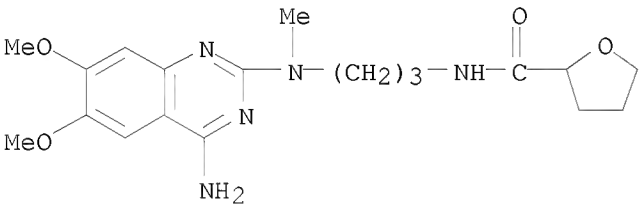
AB Acute urinary retention caused by bladder outlet obstruction resulting from prostatic enlargement is one of the commonest causes for acute admission to urol. wards. More recently, there has been a trend to commence treatment with α-blockers after catheterization followed by a trial without catheter (TWOC), in the hope that surgery may be avoided in a significant proportion of patients. There is no conclusive evidence

of the efficacy of this treatment. We conducted a study to evaluate the efficacy of using the α-blocker alfuzosin SR in patients with acute urinary retention. All patients presenting with acute urinary retention to our unit were included in the trial. Exclusion criteria included patients with known bladder or prostate malignancy, bladder calculi, urinary tract infections, urethral stricture or patients on α-blockers. A total of 81 patients consented and were randomized. Sixty-two patients completed the study. The retention volume was recorded. Trial medicine was recorded on a twice-daily dose and the first TWOC was carried out after a min. of three doses or 36 h after admission. TWOC was considered successful on voiding with a residual volume of <200 mL. Unsuccessful patients were recatheterized and discharged home on trial medication, and called for a second TWOC after 2 wk. Successful patients were continued on α-blockers and failures were put on the operating list for TURP. Patients on active treatments were reviewed at 2 yr. Of the 34 patients treated with alfuzosin SR, 17 (50%) resumed voiding and of the 28 patients from placebo group, 16 (57%) voided successfully. All 33 patients were continued open labeled on alfuzosin SR 5 mg BD. Out of 33 patients, 13 (43%) had TURP within first year after TWOC and three died due to various medical causes. Out of remaining 17 patients, 15 attended for follow-up. The mean peak flow rate was 8.4 mL/s and the mean residual volume was 112 mL. Six patients (40%) required TURP for severe lower urinary tract symptoms (LUTS). So out of 28 patients followed at 2 yr, 19 (68%) had TURP. These data do not support the routine use of α-blockers in patients with acute urinary retention. Also continuing use of α-blockers does not seem to prevent further requirements of TURP, although larger studies are needed to support this.

IT 81403-80-7, Alfuzosin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alfuzosin SR in patients undergoing trial without catheter following acute urinary retention)

RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 16 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:840542 CAPLUS

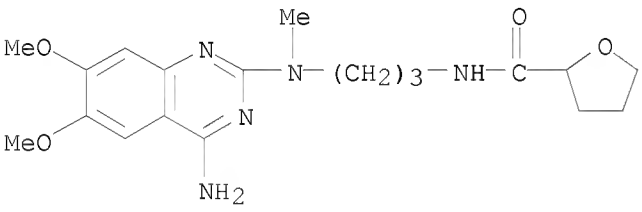
DOCUMENT NUMBER: 137:345834

TITLE: Study of the association between ischemic heart disease and use of alpha-blockers and finasteride indicated for the treatment of benign prostatic hyperplasia

AUTHOR(S): Souverein, P. C.; Herings, R. M. C.; Man in 't Veld, A. J.; De la Rosette, J. J. M. C. H.; Farmer, R. D. T.; Leufkens, H. G. M.

CORPORATE SOURCE: Department of Pharmacoepidemiology and

Pharmacotherapy, Utrecht Institute for Pharmaceutical Sciences (UIPS), Utrecht University, Utrecht, 3508 TB, Neth.
SOURCE: European Urology (2002), 42(3), 254-261
CODEN: EUURAV; ISSN: 0302-2838
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Objective: Given the high possibility of co-occurrence of benign prostatic hyperplasia (BPH) and cardiovascular disease, we evaluated whether patients using BPH drugs are at an increased risk of acute hospital admission for ischemic heart disease (IHD). Methods: A nested case control study within a cohort of 4414 men (aged ≥30 yr) who had a history of using BPH products between 1992 and 1998 was conducted. Cases were defined as men with a first record of an acute hospital admission for IHD during the study period; three controls were matched to each case on year of birth, pharmacy and calendar time (index date). Results: The study population comprised 220 cases and 515 controls. Current use of alpha-blockers (adjusted odds ratio 1.0, 95% confidence interval: 0.5-2.2) or finasteride (adjusted odds ratio 0.3, 95% CI: 0.1-1.4) was not associated with hospital admission for IHD. Furthermore, current use of BPH drugs was not associated with IHD in patient subgroups (age, history of cardiovascular disease, diabetes), nor with duration of use prior to hospitalization. Conclusion: Although the power of the study was low, we found no evidence for an association between current use of BPH drugs and hospital admission for IHD. Therefore, our study seems to confirm the good cardiovascular safety profile of modern BPH drugs.
IT 81403-68-1, Xatral
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(association between ischemic heart disease and use of alpha-blockers and finasteride (Proscar) indicated for treatment of benign prostatic hyperplasia patients)
RN 81403-68-1 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro-, hydrochloride (1:1) (CA INDEX NAME)

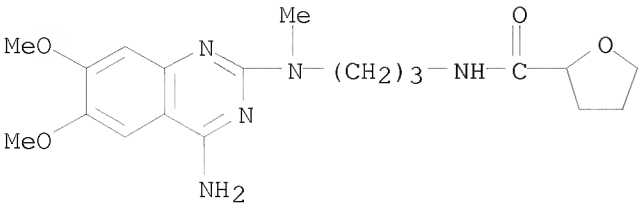


● HCl

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 17 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:799101 CAPLUS
DOCUMENT NUMBER: 137:288688
TITLE: The efficacy of alfuzosin treatment in patients with prostatism

AUTHOR(S): Basar, M. Murad; Atan, Ali; Ozergin, Osman; Yildiz, Muslum
CORPORATE SOURCE: Department of Urology Clinic, Ankara Numune Education and Research Hospital, Ankara, Turk.
SOURCE: International Urology and Nephrology (2002), Volume Date 2001, 33(3), 493-497
CODEN: IURNAE; ISSN: 0301-1623
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Alfuzosin, a quinazoline derivative, is a selective alpha-1a adrenoceptor antagonist with further selectivity for the alpha-1 adrenoceptors of the lower urinary tract and lesser affinity for vascular alpha-1 adrenoceptors. The present study evaluates the efficacy of alfuzosin in a group of the patients with prostatism. Eighty-two patients with lower urinary tract symptoms aged from 55 to 76 yr (mean age 62.36±6.4) were enrolled in the study. The patients were evaluated by blood pressure measurement, digital rectal examination, serum total and free prostate specific antigen (PSA) detns. by Tandem R-Assay with the reference range of 0.0 to 4.0 ng/mL, international prostate symptom score (IPSS), volume measurement by transrectal prostate ultrasound, blood biochem., uroflowmetry, post-voiding residual urine (PVRU) assessment. The patients treated with alfuzosin 2.5 mg three times a day for 3 mo were re-evaluated by blood pressure measurement, IPSS, urine flow rate (UFR) and PVRU assessment in the 2nd week and in the 6th week, and by blood pressure measurement, IPSS, blood biochem., serum total and free PSA detns., UFR and PVRU assessment in the 3rd month. Statistical anal. was performed using student-t test, and p value was considered significant when less than 0.05. Although IPSS significantly decreased in the 2nd week of the treatment compared to pre-treatment value, it reached a maximum decrease in the 6th week of the treatment. There were statistically significant difference between in the 2nd week IPSS value and the 6th week IPSS value. However, no difference was seen between the 6th week IPSS value and the 3rd month IPSS value. No significant difference was observed between pre-treatment values and the 2nd week values regarding UFR and PVRU. Peak flow rate and PVRU significantly changed in the 6th week of the treatment and they reached maximum change in the 3rd month. Difference was also significant between the values in the 6th week of the treatment and those in the 3rd month of the treatment. According to the blood biochem. anal., total and free PSA levels before and after the treatment, there were no significantly difference. Addnl., alfuzosin had no effect on blood pressure. Before, during and after the treatment, blood pressure did not change significantly. Present study showed that symptomatic improvement with alfuzosin treatment began in the 2nd week, reaching the maximum level in the 6th week whereas urodynamic parameters began to improve in the 6th week and reached the maximum level in the 3rd month with no effect on blood pressure and blood biochem. test.
IT 81403-80-7, Alfuzosin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(efficacy of alfuzosin treatment in patients with prostatism)
RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



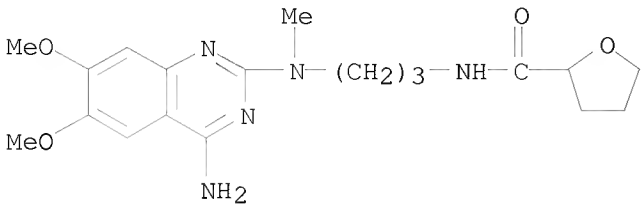
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 18 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:652133 CAPLUS
DOCUMENT NUMBER: 138:198371
TITLE: Alfuzosin, an α1-adrenoceptor antagonist for the treatment of benign prostatic hyperplasia: once daily versus 3 times daily dosing in healthy subjects
AUTHOR(S): Ahtoy, P.; Chretien, P.; Dupain, T.; Rauch, C.; Rouchouse, A.; Delfolie, A.
CORPORATE SOURCE: CeMax:3, Rouen, Fr.
SOURCE: International Journal of Clinical Pharmacology and Therapeutics (2002), 40(7), 289-294
CODEN: ICTHEK; ISSN: 0946-1965
PUBLISHER: Dustri-Verlag Dr. Karl Feistle
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Objective: Anew patented prolonged release formulation of the α1-adrenoceptor antagonist alfuzosin has been developed for once-daily (OD) administration in benign prostatic hyperplasia (BPH). This study was designed to compare 2 dose regimens: 10 mg OD alfuzosin and 2.5 mg TID alfuzosin at steady state. Methods: In an open, randomized crossover study with a 9-day washout between treatments, 18 healthy male subjects (50-65 yr) received OD or TID alfuzosin tablets orally over 5 days. Both formulations were administered according to the schedule recommended for therapeutic use: OD was administered 5 min after the evening meal, TID was administered in the evening, then in the morning and at noon (30 min before meals). On the fifth day, plasma concns. were quantitated by HPLC with spectrofluorometric detection. Results: The following pharmacokinetic parameters refer to the geometric mean values for both formulations. Mean Cmax value of 10 mg OD alfuzosin was 15.8 ng/mL at a median tmax of 9.0 h; Cmax was higher and reached earlier from 2.5 mg alfuzosin t.i.d: 19.3 ng/mL, 19.7 ng/mL and 20.3 at 1.0 h after each dosing, resp. Mean AUC(0-24) values after OD and TID were 228.3 and 226.0 ng + h/mL, resp. Based on AUC(0-24) values corrected by the administered daily dose, the relative bioavailability of alfuzosin OD was 75.7% with a 90% confidence interval of 68.0-84.3%. Non-corrected AUC(0-24) values were bioequivalent with a ratio estimate of 101.0% and a 90% confidence interval of 90.7 - 112.5%. The higher daily dose compensated for the loss of bioavailability observed with the OD formulation. Mean t1/2z value was longer for the OD (8.9 h) than the TID formulation (6.9 h). Variability between individuals was similar for the 2 formulations. Both dose regimens were well tolerated. Conclusions: Alfuzosin 10 mg once-daily provides a suitable pharmacokinetic profile for a once-daily administration; equivalent bioavailability between the 2 dosage regimens and a good safety profile justify the use of alfuzosin 10 mg inpatients with BPH.

IT 81403-80-7, Alfuzosin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

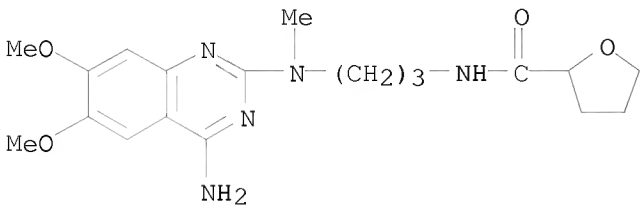
(Biological study); USES (Uses)
(alfuzosin for treatment of benign prostatic hyperplasia)
RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

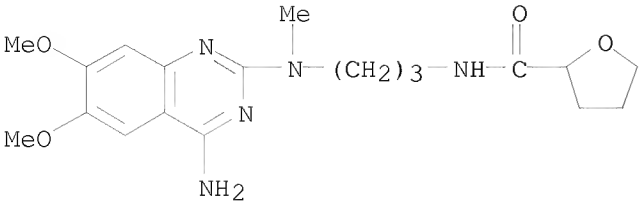
L5 ANSWER 19 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:562993 CAPLUS
DOCUMENT NUMBER: 137:134975
TITLE: Selective serotonin reuptake inhibitor-induced urinary incontinence
AUTHOR(S): Movig, K. L. L.; Leufkens, H. G. M.; Belitser, S. V.; Lenderink, A. W.; Egberts, A. C. G.
CORPORATE SOURCE: Hospital Pharmacy Midden-Brabant, TweeSteden Hospital and St. Elisabeth Hospital, Tilburg, Neth.
SOURCE: Pharmacoepidemiology and Drug Safety (2002), 11(4), 271-279
CODEN: PDSAEA; ISSN: 1053-8569
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Irresp. of its cause, urinary incontinence is a medical condition seriously affecting quality of life and is increasingly recognized. In this study, we examined the association between the use of selective serotonin reuptake inhibitors (SSRIs) and urinary incontinence. A retrospective follow-up study among starters with an SSRI was performed to estimate the relative and absolute risk for urinary incontinence associated with SSRI use. Data came from the PHARMO database, which includes information on drug dispensing for approx. 450 000 residents living in eight Dutch cities. All patients initially using an SSRI between 1994 and 1998 were selected. The frequency measures for urinary incontinence were estimated by using prescription sequence anal., where initiation of spasmolytic drugs or absorbent products was used as a measure for urinary incontinence. Besides crude incidence d. calcns., Andersen-Gill's model was used in order to control for possible confounding factors and time varying covariates. A total of 13 531 were identified as first time users of an SSRI. Compared to non-exposure, the incidence d. ratio for urinary incontinence during SSRI exposure was 1.75 (95% CI 1.56-1.97). Overall, compared to baseline, SSRI use caused 14 extra cases of urinary incontinence per 1000 patients treated per yr; the elderly were more at risk resulting in 60 extra cases per 1000 patients per yr. The adjusted relative risk for urinary incontinence due to SSRI use was 1.61 (95% CI 1.42-1.82); the risk for sertraline users was 2.76 (95% CI 1.47-5.21). Exposure to SSRIs is associated with an increased risk for developing urinary incontinence, which can be explained pharmacol. Approx. 15 out of 1000 patients treated per yr with an SSRI developed urinary incontinence. The elderly and users of sertraline are at the highest risk.

IT 81403-80-7, Alfuzosin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(selective serotonin reuptake inhibitor-induced urinary incontinence)
RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 20 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:556936 CAPLUS
DOCUMENT NUMBER: 137:269647
TITLE: Voltammetric analysis of alfuzosin HCl in pharmaceuticals, human serum and simulated gastric juice
AUTHOR(S): Uslu, Bengi
CORPORATE SOURCE: Faculty of Pharmacy, Department of Analytical Chemistry, Ankara University, Ankara, 06100, Turk.
SOURCE: Electroanalysis (2002), 14(12), 866-870
CODEN: ELANEU; ISSN: 1040-0397
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The electrochem. oxidation of alfuzosin was investigated by cyclic, linear sweep, differential pulse and square-wave voltammetry at glassy carbon disk electrode. Alfuzosin hydrochloride showed a well-defined anodic wave in Britton-Robinson and phosphate buffers over the pH range 2-7.5. For anal. purposes, a very well resolved diffusion controlled voltammetric peak was obtained in phosphate buffer at pH 6.0 for differential pulse and square-wave voltammetric techniques. The linear response was obtained in the ranges of 6 + 10-7 M - 1 + 10-4 M for both techniques. Detection limits were found 1.56 + 10-7 M for DPV and 6.2 + 10-8 M for SWV. Based on this study, simple, rapid, selective and sensitive two voltammetric methods were developed for the determination of the alfuzosin in tablet dosage form, human serum and simulated gastric juice.
IT 81403-68-1, Alfuzosin hydrochloride
RL: ANT (Analyte); CPS (Chemical process); PEP (Physical, engineering or chemical process); RCT (Reactant); ANST (Analytical study); PROC (Process); RACT (Reactant or reagent)
(voltammetric anal. in pharmaceuticals, human serum and simulated gastric juice)
RN 81403-68-1 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 21 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:552326 CAPLUS
DOCUMENT NUMBER: 137:99037
TITLE: Method for treating benign prostate hyperplasia
INVENTOR(S): Lawyer, Carl H.
PATENT ASSIGNEE(S): Upsher-Smith Laboratories, Inc., USA
SOURCE: U.S., 10 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

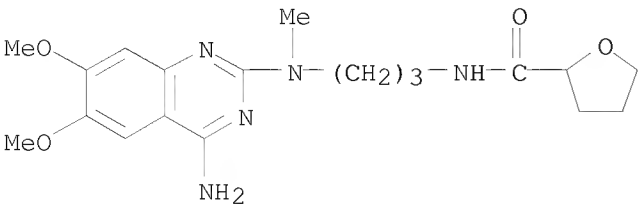
PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 6423719	B1	20020723	US 2000-505220		20000216
PRIORITY APPLN. INFO.:			US 1999-120099P	P	19990216

OTHER SOURCE(S): MARPAT 137:99037

AB Disclosed is a method of symptomatic treatment of benign prostatic hyperplasia in a subject, comprising: administering to a subject in need thereof, an effective amount of a xanthine derivative Administration of dyphylline in a sustained release oral dosage form is preferred. A sustained-release tablet was formulated containing dyphylline 400, hydroxypropyl Me cellulose 95, Povidone 32, silica 2, and Mg stearate mg/tablet.

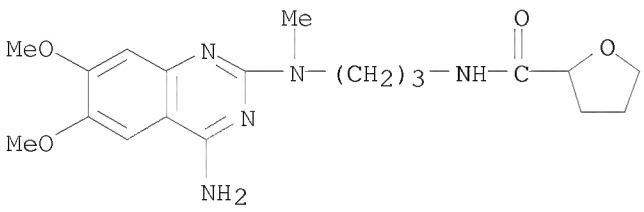
IT 81403-80-7, Alfuzosin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral prepns. containing xanthine derivs. and other active agents for treating benign prostate hyperplasia)

RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 22 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:460603 CAPLUS
DOCUMENT NUMBER: 138:100286
TITLE: Determination of alfuzosin in human plasma by RP-HPLC with fluorometric detection
AUTHOR(S): Yao, Hongwei; Jin, Yong; Li, Jun; Zhang, Yunfang; Ding, Xiunian; Xu, Shuyun
CORPORATE SOURCE: Institute of Clinical Pharmacology, Anhui Medical University, Hefei, 230032, Peop. Rep. China
SOURCE: Yaowu Fenxi Zazhi (2002), 22(2), 127-129
CODEN: YFZADL; ISSN: 0254-1793
PUBLISHER: Yaowu Fenxi Zazhi Bianji Weiyuanhui
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB A RP-HPLC method for determination of alfuzosin in human plasma was established.
The chromatog. column was a Shimadzu C18 column (150 mm x 4.6 mm). The mobile phase consisted of 0.02 mol L-1 phosphate buffer (pH 2.5)-acetonitrile (40 : 60) with a flow rate of 1.0 mL min-1. The fluorimetric excitation and emission wavelengths were set at 374 nm and 378 nm, resp. The serum samples were alkalized with NaOH and extracted with di-Et ether. The organic phase was evaporated to dryness with N2 stream, and the residues were dissolved with 0.02 mol L-1 phosphate buffer (pH 2.5)-acetonitrile (90 : 10). Alfuzoisn was well separated and obvious interactive peak in plasma was not observed The results of detection could represent concentration of primary drug. The lowest concentration of detection was 0.78 ng mL-1, the lowest limit of detection was 39 pg. The linear ranges was 0.78-50 ng mL-1, the linear regression equation was Y = 8 648.7X + 767.8 ($r = 0.999$, $P < 0.05$). Recovery ratio of extraction was > 70%, RSD of intra-day and inter-day was < 10%. All of those satisfied anal. requirement of biol. preparation
IT 81403-80-7, Alfuzosin
RL: ANT (Analyte); ANST (Analytical study)
(determination of alfuzosin in human plasma by RP-HPLC with fluorometric detection)
RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



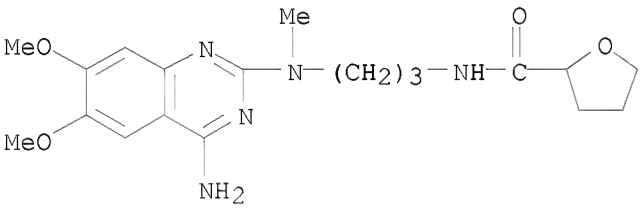
L5 ANSWER 23 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:431468 CAPLUS
DOCUMENT NUMBER: 137:41204
TITLE: Alfuzosin: A clinically uroselective α1-blocker

AUTHOR(S): Hofner, Klaus; Jonas, Udo
CORPORATE SOURCE: Evang. Krankenhaus Oberhausen, Urologische Klinik, Oberhausen, 46047, Germany
SOURCE: World Journal of Urology (2002), 19(6), 405-412
CODEN: WJURDJ; ISSN: 0724-4983
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. A once-daily (o.d.) formulation of alfuzosin has recently been developed in order to improve the convenience of dosing and to provide optimal pharmacokinetic coverage over a 24-h period. The results of two double-blind, placebo-controlled phase III studies of similar design that included 983 patients with LUTS that suggested BPH have confirmed that alfuzosin 10 mg o.d. is a 24-h effective treatment for both symptoms and flow rates, and that there is no addnl. benefit in using a higher dosage. In addition, alfuzosin is the only α1-blocker that has demonstrated a significant decrease in post-void residual urine, a known risk factor for acute urinary retention, as well as the incidence of acute urinary retention in comparison with a placebo. Administered without an initial dose titration, alfuzosin 10 mg o.d. is well tolerated, with a low incidence of postural hypotension (<1%) and no significant changes in blood pressure compared with a placebo, even in elderly and hypertensive patients. Ejaculation disorders were rarely reported and did not show an evident causal relationship to treatment. Alfuzosin 10 mg o.d. also exhibits an excellent sexual side-effect profile, with no deleterious impact on this important aspect of quality of life for BPH patients.

IT 81403-80-7, Alfuzosin
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alfuzosin: uroselective α1-blocker for patients with benign prostatic hyperplasia (BPH))

RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 24 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:392232 CAPLUS
DOCUMENT NUMBER: 136:401912
TITLE: Nitrosated and nitrosylated alpha-adrenergic receptor antagonist compounds, compositions and their uses
INVENTOR(S): Garvey, David S.; Schroeder, Joseph D.; Saenz de Tejada, Inigo
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 40 pp., Cont.-in-part of U.S. Ser. No. 714,313.
CODEN: USXXCO

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20020061879	A1	20020523	US 2001-24550	20011221
US 5932538	A	19990803	US 1996-595732	19960202
US 5994294	A	19991130	US 1996-714313	19960918
PRIORITY APPLN. INFO.:			US 1996-595732	A2 19960202
			US 1996-714313	A2 19960918

OTHER SOURCE(S): MARPAT 136:401912
GI

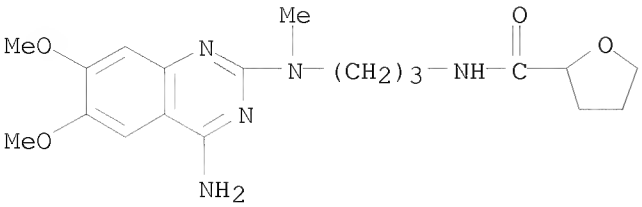
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention is directed to nitrosated or nitrosylated a-adrenergic receptor antagonists, e.g. I [Ra = H, alkoxy; Rb = NMe(CH2)aNHCORc, 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-2-yl; a= 2, 3; Rc = heteroaryl, heterocycle, lower alkyl, hydroxyalkyl, arylheterocycle; D = NO, NO2, C(Rd)OC(O)YZ(CReRf)pTQ; Rd = H, lower alkyl, cycloalkyl, aryl aralkyl, heteroaryl; Y = O, S, C, NRi; Ri = H, lower alkyl; Re, Rf = H, lower alkyl, haloalkyl, cycloalkyl, alkoxy, aryl, heteroaryl, NH2, (di)alkylamino, amido, CO2H, ester, TQ; ReRf = carbonyl, heterocycle, cycloalkyl; p = 1 - 10; T = bond, O, S, N; Z = bond, lower alkyl, haloalkyl, cycloalkyl, aryl, (CReRf)p, Q = NO, NO2], II [R = CH2N(C6H4Me-4)C6H4OD1-3, CH2Ph, 2-methoxy-1,4-benzodioxin-2-yl, 1-methyl-2,3-dihydroisoindol-2-yl, 5-chloro-2,3-dihydroisoindol-2-yl; D1 = H, D], III [Rh = H, C(O)ORd, C(O)X; X = Y(CReRf)pG(CReRf)pTQ; G = bond, TC(O), C(O)T, C{YC(O)Rm}; Rm = heteroaryl, heterocycle], IV [A1 = O, CH2], V, (RmRkC)N(D1)(CRkRl) [Rk = H, lower alkly; Rl = CH2C6H4O(CH2)bMe, CH2C6H4OD, CH2OC6H3(OMe)2-2,6, CH2CH2Ph; b = 0, 1; Rn = CH2C6H4(SO2NH2)-3, 1-oxotetralin-2-yl, 1,4-benzodioxin-2-yl] and RpRkCHCH(Ro)OD [Ro = (1-naphthyloxy)methyl, C6H4OD1; Rp = 4-benzylpiperidino, 4-(2-methoxyphenyl)piperazino]. The present invention is also directed to compns. comprising α-adrenergic receptor antagonists that are optionally substituted with at least one NO or NO2 moiety and compds. that donate, transfer or release nitric oxide or elevate levels of endogenous endothelium-derived relaxing factor, and methods for treating sexual dysfunctions in males and females. Thus, S-Nitrosoglutathione was prepared from glutathione via reaction with NaNO2 in aqueous HCl. S-Nitrosoglutathione at 500 μg was able to induce near maximal erectile response in anesthetized rabbits.

IT 81403-80-7D, Alfuzosin, nitrosated or nitrosylated
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of nitrosated and nitrosylated alpha-adrenergic receptor antagonist compds., compns. and their uses)

RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)

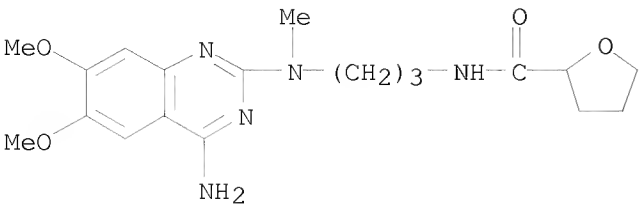


L5 ANSWER 25 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:314180 CAPLUS
DOCUMENT NUMBER: 136:395661
TITLE: Long-term safety and efficacy of a once-daily formulation of alfuzosin 10 mg in patients with symptomatic benign prostatic hyperplasia: Open-label extension study
AUTHOR(S): Van Kerrebroeck, P.; Jardin, A.; Van Cangh, P.; Laval, K. U.
CORPORATE SOURCE: Department of Urology, Academisch Ziekenhuis Maastricht, Maastricht, NL-6202 AZ, Neth.
SOURCE: European Urology (2002), 41(1), 54-61
CODEN: EUURAV; ISSN: 0302-2838
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Objectives: To evaluate the long-term safety and efficacy of a new, once-daily (o.d.) prolonged-release formulation of the clin. uroselective α1-blocker, alfuzosin, in patients with symptomatic benign prostatic hyperplasia (BPH). Methods: This is a 9-mo open-label extension of a 3-mo double-blind, placebo-controlled evaluation of alfuzosin 10 mg o.d. and standard alfuzosin 2.5 mg, three times daily (t.i.d.), administered without dose titration in both cases. A total of 311 patients continued in the extension phase and all received alfuzosin 10 mg o.d. Efficacy was evaluated in all patients enrolled in the extension phase (n = 311). Safety was assessed in all patients exposed to alfuzosin, whether in the double-blind or extension phase (n = 360). Results: Mean international prostate symptom score (IPSS) improved significantly, from 17.1 to 9.3 (P < 0.0001), and mean peak flow rate (PFR) (assessed at through plasma levels) increased significantly, from 9.1 to 11.3 mL/s (P < 0.0001), between baseline (i.e., beginning of the double-blind phase) and the endpoint of the extension phase. Quality of life (QOL) index also improved significantly, from 3.3 to 2.1 (P < 0.0001). Alfuzosin was well tolerated, with only 16 of 360 patients (4.4%) reporting adverse events potentially related to α-blockade (mainly dizziness). Ejaculation disorders were infrequent (0.6%) and did not show a relationship to treatment. The incidence of asymptomatic orthostatic hypotension was low (2.8%), and no age effect was identified. Conclusions: Alfuzosin 10 mg o.d. provides effective relief from BPH, and clin. benefits are maintained up to 12 mo. This study also demonstrates the satisfactory long-term safety of this formulation, and its safe use even in at-risk populations.

IT 81403-80-7, Alfuzosin
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(long-term safety and efficacy of once-daily formulation of alfuzosin in humans with symptomatic benign prostatic hyperplasia)

RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



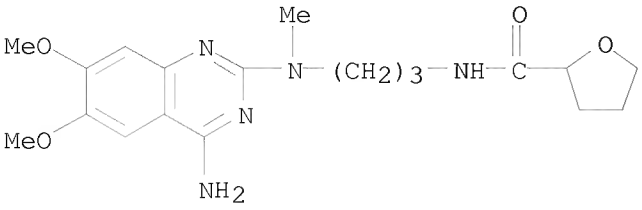
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 26 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:311088 CAPLUS
DOCUMENT NUMBER: 136:380005
TITLE: Drug or symptom-induced depression in men treated with alpha1-blockers for benign prostatic hyperplasia? A nested case-control study
AUTHOR(S): Clifford, Gary M.; Farmer, Richard D. T.
CORPORATE SOURCE: Department of Pharmacoepidemiology and Public Health, Postgraduate Medical School, University of Surrey, Guildford, GU2 7DJ, UK
SOURCE: Pharmacoepidemiology and Drug Safety (2002), 11(1), 55-61
CODEN: PDSAEA; ISSN: 1053-8569
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Regulatory authorities have raised concern that α1-blockers, prescribed predominantly for benign prostatic hyperplasia (BPH), may be associated with an increased risk of depression. The aim was to assess the risk of depression with α1-blockers independently of that associated with symptoms being treated and concurrent illness. Using a study population registered on the UK General Practice Research Database, and taking a prescription for an antidepressant as a proxy for clin. depression, we performed: (a) cohort analyses comparing the incidence of depression in current users of α1-blockers vs. non-users, and in men with BPH vs. those without. (b) A nested case-control anal. looking at the association between depression and α1-blocker exposure, accounting for the presence of BPH and other illness. In the cohort analyses, risk of depression was significantly higher in men with BPH compared to those without (IRR 2.17, 2.12-2.22), but was not significantly different for men exposed to α1-blockers vs. those unexposed when adjusted for the presence of BPH. Cases of depression were more likely to have pre-existing BPH (crude OR 2.09, 2.02-2.15) than controls. After adjusting for concurrent illness (using number of GP visits as a proxy) and the presence of BPH (adjusted OR 1.38, 1.33-1.43), there was no association with depression for exposure to any α1-blocker (adjusted OR 1.03, 0.90-1.18). This study did not suggest that the prescribing of α1-blockers increases the risk of being depressed. The association highlighted by spontaneous reporting systems appears to be explained by confounding by concurrent disease.

IT 81403-80-7, Alfuzosin
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(depression risk in men treated with alpha1-blockers for benign prostatic hyperplasia)
RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



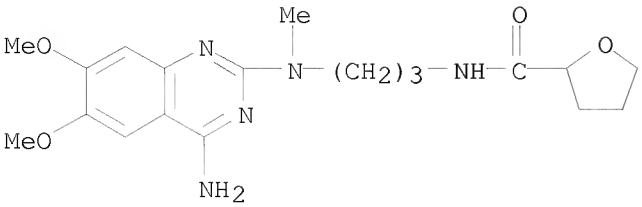
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 27 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:304360 CAPLUS
DOCUMENT NUMBER: 136:363169
TITLE: Alfuzosin: a review of the therapeutic use of the prolonged-release formulation given once daily in the management of benign prostatic hyperplasia
AUTHOR(S): McKeage, Kate; Plosker, Greg L.
CORPORATE SOURCE: Adis International Limited, Auckland, N. Z.
SOURCE: Drugs (2002), 62(4), 633-653
CODEN: DRUGAY; ISSN: 0012-6667
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Data Selection Sources included medical literature published in any language since 1983 on alfuzosin, identified using AdisBase (a proprietary database of Adis International), Medline and EMBASE. Addnl. refs. were identified from the reference lists of published articles. Bibliog. information, including contributory unpublished data, was also requested from the company developing the drug. AdisBase search terms were "alfuzosin" and "benign-prostatic-hyperplasia" or "alfuzosin PK/PD". Medline search terms were "alfuzosin" and "prostatic-hyperplasia". EMBASE search terms were "alfuzosin" or "SL 77499" and "prostate-hypertrophy". Searches were last updated 3 Jan. 2002. Studies in patients with benign prostatic hyperplasia who received prolonged-release alfuzosin 10mg. Inclusion of studies was based mainly on the methods section of the trials. When available, large, well controlled trials with appropriate statistical methodol. were preferred. Relevant pharmacodynamic and pharmacokinetic data are also included.

IT 81403-80-7, Alfuzosin
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alfuzosin prolonged-release formulation given once daily in management of benign prostatic hyperplasia)

RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



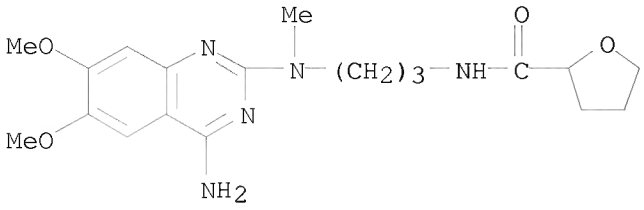
REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 28 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:277537 CAPLUS
DOCUMENT NUMBER: 136:363752
TITLE: Long-term risk of re-treatment of patients using α-blockers for lower urinary tract symptoms
AUTHOR(S): De La Rosette, Jean J. M. C. H.; Kortmann, Barbara B. M.; Rossi, Cristina; Sonke, Gabe S.; Floratos, Diamandis L.; Kiemeney, Lambertus A. L. M.
CORPORATE SOURCE: Departments of Urology and Epidemiology, University Medical Centre St. Radboud, Nijmegen, Neth.
SOURCE: Journal of Urology (Hagerstown, MD, United States) (2002), 167(4), 1734-1739
CODEN: JOURAA; ISSN: 0022-5347
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The efficacy of α-adrenoceptor blockers for the treatment of lower urinary tract symptoms has been proven in numerous studies. However, little is known about the efficacy of the longer term. We investigated the long-term risk of re-treatment in patients using α-adrenoceptor blockers for lower urinary tract symptoms and the parameters that influence this risk. We reviewed the files of 316 patients with lower urinary tract symptoms treated at our department with the α-blockers terazosin, alfuzosin or tamsulosin. Using follow up data up to 3 yr, we calculated re-treatment percentages in each treatment group. Using extended follow up of 5 yr, we calculated the predictive value of various baseline characteristics for re-treatment. The re-treatment rates were 27% for tamsulosin, 37% for alfuzosin and 49% for terazosin. The re-treatment rates of patients with mild, moderate and severe lower urinary tract symptoms were 27%, 33% and 70%, resp. Patients with a maximum urine flow of less or more than 10 mL. per s had a re-treatment rate of 58% and 47%, resp. Patients with a prostate volume of less or more than 40 mL. had a re-treatment rate of 48% and 72%, resp. Patients who were urodynamically unobstructed vs. obstructed patients had a re-treatment rate of 44% and 59%, resp. Patients given α-blockers for lower urinary tract symptoms have a high risk of re-treatment. Tamsulosin has a markedly lower re-treatment percentage than alfuzosin and terazosin. Severe symptoms, poor urine flow, an enlarged prostate and urodynamically proven bladder outlet obstruction increase the risk of treatment failure. Preselection of the most suitable candidates for α-blockade may reduce this risk.

IT 81403-80-7, Alfuzosin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(re-treatment of patients using α-blockers for lower urinary tract symptoms)
RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 29 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:205190 CAPLUS
DOCUMENT NUMBER: 136:319125
TITLE: Terazosin for treating symptomatic benign prostatic obstruction: A systematic review of efficacy and adverse effects
AUTHOR(S): Wilt, T. J.; Howe, W.; MacDonald, R.
CORPORATE SOURCE: The Cochrane Review Group in Prostate Diseases and Urologic Cancers, VA Medical Center, Minneapolis VA Center for Chronic Disease Outcomes Research, Minneapolis, USA
SOURCE: BJU International (2002), 89(3), 214-225
CODEN: BJINFO; ISSN: 1464-4096
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

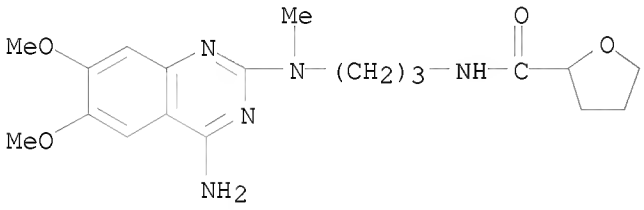
AB The aim of this study was to systematically review and evaluate the effectiveness and adverse effects of the α-antagonist, terazosin, for treating urinary symptoms associated with benign prostatic obstruction (BPO). Studies were sought and included in the review if they were randomized trials of at least 1 mo duration, involved men with symptomatic BPO and compared terazosin with placebo or active controls. The study, patient characteristics and outcome data were extracted in duplicate onto standardized forms using a prospectively developed protocol. Seventeen studies involving 5151 men met the inclusion criteria, i.e. placebo-controlled (10), α-blockers (seven), finasteride alone or combined with terazosin and placebo (one), and microwave therapy (one). The study duration was 4-52 wk; the mean age of the men was 65 yr and 82% were white. Baseline urol. symptom scale scores and flow rates showed that men had moderate BPO. Efficacy outcomes were rarely reported in a way that allowed for data pooling, but indicated that terazosin improved symptom scores and flow rates more than did placebo or finasteride, and similarly to other α-antagonists. The pooled mean percentage improvement for the Boyarsky symptom score was 37% for terazosin and 15% for placebo (four studies). The mean percentage improvement for the American Urol. Association symptom score was 38%, compared with 17% and 20% for placebo and finasteride, resp. (two studies). The pooled mean improvement in the International Prostate Symptom Score of 40% was similar to that with tamsulosin (43%). Peak urinary flow rates improved more with terazosin (22%) than with placebo (11%) and finasteride (15%), but did not differ significantly from the other α-antagonists. The percentage of men discontinuing terazosin was comparable with those receiving placebo and finasteride, but greater than with other α-antagonists. Adverse effects were greater than with placebo and included dizziness, asthenia,

headache and postural hypotension. The available evidence indicates that terazosin improves the symptoms and flow rates associated with BPO; it was more effective than placebo or finasteride and similar to other α-antagonists. Adverse effects were generally mild but more frequent than with other α-antagonists and associated with a two- to four-fold increase in treatment discontinuation.

IT 81403-80-7, Alfuzosin
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(terazosin for treating symptomatic benign prostatic obstruction)

RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 30 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:81271 CAPLUS

DOCUMENT NUMBER: 136:252612

TITLE: Oscillopolarographic determination of alfuzosin and its electrochemical behavior

AUTHOR(S): Cao, Erxin; Zeng, Yonghuai

CORPORATE SOURCE: Department of Chemistry, Beijing Normal University, Beijing, 100875, Peop. Rep. China

SOURCE: Zhongguo Yaoxue Zazhi (Beijing, China) (2001), 36(11), 763-766
CODEN: ZYZAEU; ISSN: 1001-2494

PUBLISHER: Zhongguo Yaoxue Zazhishe

DOCUMENT TYPE: Journal

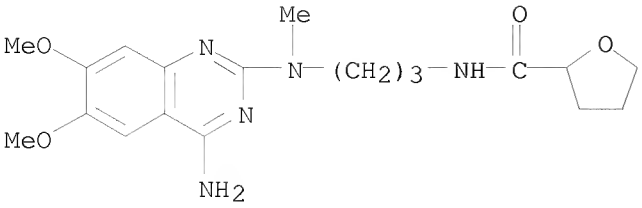
LANGUAGE: Chinese

AB The electrochem. behavior and reduction mechanism of alfuzosin (AFZ) in phosphate buffer solution were studied. A new method for the determination of AFZ was established by single-sweep oscillopolarog. and cyclic voltammetry. In a supporting electrolyte of 0.01 mol L-1 KH2PO4-K2HPO4 (pH 7.05), a sensitive derivative reduction peak of AFZ was found by single-sweep oscillopolarog. THe peak potential was -1.60 V (vs. SCE). The relationship between peak height and the concentration of AFZ was linear in the range 1.0 x 10-7-9.0 x 10-6 mol L-1. The detection limit was 3.0 x 10-8 mol L-1. The method was applied to determine AFZ in tablets with satisfactory results. This indicated an irreversible process with adsorption.

IT 81403-80-7, Alfuzosin
RL: ANT (Analyte); PRP (Properties); ANST (Analytical study)
(oscillopolarog. determination of alfuzosin and its electrochem. behavior)

RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



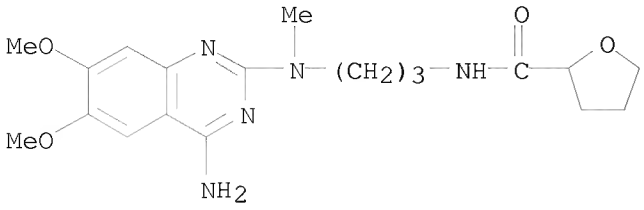
L5 ANSWER 31 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:71477 CAPLUS
DOCUMENT NUMBER: 137:179134
TITLE: Initial Choices and Final Outcomes in Lower Urinary Tract Symptoms
AUTHOR(S): Speakman, Mark J.
CORPORATE SOURCE: Taunton and Somerset NHS Trust, Taunton, UK
SOURCE: European Urology (2001), 40(Suppl. 4), 21-30
CODEN: EUURAV; ISSN: 0302-2838
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Management of lower urinary tract symptoms (LUTS) suggestive of benign prostatic hyperplasia (BPH) requires careful thought so that the most appropriate treatment can be targeted to each individual patient. Initial choices in the management of LUTS/BPH include watchful waiting, medical therapies and surgical interventions. A decision on treatment choice should be taken together with the patient. It should be based on the best available scientific evidence but also be individualized to patients' circumstances and personal choices. Management of LUTS/BPH should be focused on the burden and impact of urinary symptoms and related quality of life. The rate of treatment failure, which can be assessed through the switch to other medical therapy or surgery and/or the delay or prevention of complications related to LUTS/BPH, is also important. Beneficial effects of treatment should be balanced against the incidence of adverse events associated with therapy. Medical therapy has been shown to be effective in improving short-term outcomes (maximum urinary flow rate and symptom scores). Increasing evidence indicates that in the long-term more selective α1-adrenoceptor (AR) antagonists such as alfuzosin and tamsulosin may reduce the risk of treatment failure with a comparable rate to finasteride. Although the different α1-AR antagonists are equivalent in efficacy they differ in tolerability with the subtype selective tamsulosin having the lowest risk for interference with blood pressure regulation. Transurethral resection of the prostate (TURP) improves storage symptoms to a lesser extent and/or more slowly than it improves voiding symptoms. In contrast, α1-AR antagonists improve both voiding and bothersome storage symptoms to the same extent and quite rapidly which has a considerable impact on quality of life. α1-AR antagonists also relieve storage symptoms to almost the same extent as TURP. Ultimately the initial choice of treatment will depend upon its efficacy, speed of onset, durability, tolerability and on patients' choice. For the majority of patients with moderate to severe symptoms a subtype selective α1-AR antagonist such as tamsulosin offers the best current combination of efficacy and tolerability.

IT 81403-80-7, Alfuzosin
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(initial choices for treatment and final outcomes in lower urinary tract symptoms)

RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



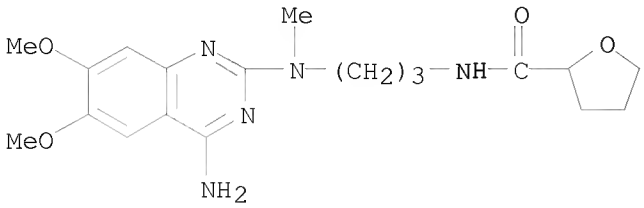
REFERENCE COUNT: 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 32 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:71476 CAPLUS
DOCUMENT NUMBER: 137:183029
TITLE: Lower Urinary Tract Symptoms: What Are the Implications for the Patients?
AUTHOR(S): Scarpa, Roberto M.
CORPORATE SOURCE: Universita di Torino, Ospedale S. Luigi Gonzaga, Orbassano, Italy
SOURCE: European Urology (2001), 40(Suppl. 4), 12-20
CODEN: EUURAV; ISSN: 0302-2838
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Patients with lower urinary tract symptoms (LUTS) suggestive of benign prostatic hyperplasia (BPH) complain about symptoms such as weak stream, dribbling, intermittency, frequency, nocturia and urgency. To effectively manage these symptoms, it is important to better understand the epidemiol. and/or the bothersomeness of these symptoms, the impact of the symptoms on the patient's quality of life and life style, when and why patients seek medical advice and the subsequent management of LUTS/BPH in clin. practice. This paper gives an overview of these issues considering 3 recently conducted European surveys. Although voiding symptoms are more frequent in patients with LUTS/BPH, storage symptoms, such as frequency, urgency, nocturia and urge incontinence, seem to be more bothersome to the patients. LUTS seem to have a neg. impact on the patient's quality of life and sexuality and to interfere strongly with daily life activities. With regard to sexuality, interference with the patient's overall sex life and erection problems is experienced as much more bothersome than ejaculation problems. After the initial symptoms, most patients postpone a visit to the physician and try to adjust their life style to self manage their symptoms. Eventually they seek medical advice because they are too much bothered by their LUTS. In Italy, medical therapy is the most frequently administered treatment option by urologists (57% of patients) followed by surgery (37% of patients). α1-Adrenoceptor antagonists are the predominant medical therapy prescribed (70% of all medically treated patients), particularly tamsulosin (35% of all medically treated patients). An interview with European urologists confirms that α1-adrenoceptor antagonists, especially newer uro-selective ones like tamsulosin, are a very appropriate initial treatment choice in the management of both voiding and storage LUTS.

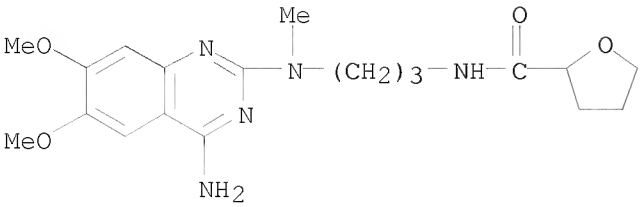
IT 81403-80-7, Alfuzosin
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(implications of lower urinary tract symptoms for patients and

treatment choices for symptom management)
RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 33 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:71474 CAPLUS
DOCUMENT NUMBER: 137:179132
TITLE: Long-Term Aspects of Medical Treatment of BPH
AUTHOR(S): Schulman, Claude C.
CORPORATE SOURCE: Department of Urology, Erasme Hospital, University Clinics of Brussels, Belg.
SOURCE: European Urology (2001), 40(Suppl. 3), 8-12
CODEN: EUURAV; ISSN: 0302-2838
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Acute urinary retention (AUR) is an important complication of benign prostatic hyperplasia (BPH) and can affect 0.4-25% of men seen in urol. practice each year. AUR is also one of the main indications for surgery, being the presenting feature of 25-30% of transurethral resection of the prostate (TURP). However, TURP conducted under these conditions is associated with higher morbidity. A number of risk factors for AUR have been identified including severity of lower urinary tract symptoms (LUTS), reduced peak flow rate, prostate volume, post-void residual volume (PVR) and old age. Medical therapy for BPH can impact on prostate size, increased PVR and previous AUR episodes. Finasteride has been shown to reduce prostate size and consequently reduce the risk of AUR. Studies on the α1 blocker, alfuzosin, also report a reduced incidence of AUR compared with placebo. In addition, alfuzosin has proven effective in a trial without catheter in patients with AUR, thus potentially reducing the need for prostate surgery or allowing elective surgery to be conducted without pre-operative catheterization. Both options are highly beneficial to the patient.
IT 81403-80-7, Alfuzosin
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(long-term aspects of medical treatment of benign prostatic hyperplasia (BPH))
RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



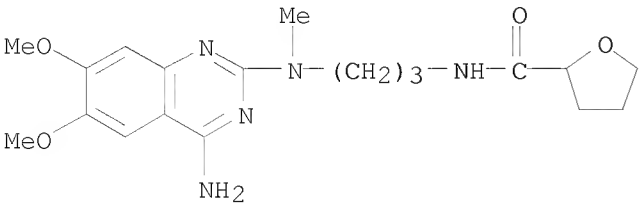
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 34 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:805073 CAPLUS
DOCUMENT NUMBER: 137:57062
TITLE: Management of Patients with LUTS Suggestive of BPH
AUTHOR(S): Gentile, Marcello; Carini, Marco; Morgia, Giuseppe; Selvaggi, Francesco Paolo; Randone, Donato; Rosati, Antonio
CORPORATE SOURCE: Azienda Sanitaria Locale, Avellino, Italy
SOURCE: European Urology (2001), 40(Suppl. 1), 5-8
CODEN: EUURAV; ISSN: 0302-2838
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The QUIBUS study offers some insights into the current diagnosis and treatment of LUTS suggestive of BPH in Italy. As diagnosis is concerned, uroflowmetry and PSA testing were performed in a high percentage of cases (64 and 89%, resp.). Both transrectal ultrasonog. and prostate biopsy were more frequent for increasing values of PSA, this suggesting that are used as screening procedures for prostate cancer. However, transrectal ultrasonog. was performed overall in a large proportion of patients (61%), representing a routine examination in some centers. As treatment is concerned, the majority of QUIBUS patients had undergone or were undergoing medical therapy. Alphalytics were the drugs most commonly prescribed by urologists while primary care physicians showed the attitude to prescribe more frequently finasteride. On the surgical side, transurethral prostatectomy and open surgery were the most commonly employed procedures, suggesting that little room is left at present to minimally invasive procedures in Italy.

IT 81403-80-7, Alfuzosin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diagnosis and therapy of patients with lower urinary tract symptoms suggestive of benign prostatic hyperplasia)

RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



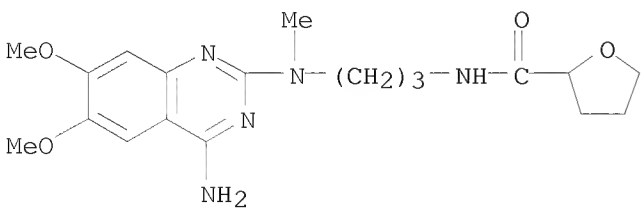
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 35 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:748254 CAPLUS
DOCUMENT NUMBER: 135:293991
TITLE: Compositions containing an α1-blocker and Saw palmetto extract for treatment of benign prostatic hypertrophy
INVENTOR(S): Hammerly, Milton
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 6 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20010028897	A1	20011011	US 2001-784584	20010215
PRIORITY APPLN. INFO.:			US 2000-183703P P	20000218

AB Compns. comprising an α1-adrenergic blocker, e.g., doxazosin, tamsulosin, and terazosin, in combination with an extract derived from the berries of the Saw palmetto plant for the treatment of benign prostatic hypertrophy are presented. The extract is typically obtained from the dried berries using extraction means known to those skilled in the art. Through use of the compns. of the invention, relaxation of the smooth muscles present in the prostate gland may be effected while simultaneously inhibiting glandular growth of the prostate thus providing a heretofore unobserved synergy in terms of relief to sufferers of benign prostatic hypertrophy. For example, 16.0 g of Saw palmetto extract containing 80.0-95.0% of fatty acids and 0.20-0.40% of sterols was dissolved in 100 mL of 90% ethanol. To this solution was added 0.10 g of bunazosin and admixt. was affected by gentle stirring of the solution Removal of the excess solvent provides a residue suitable for the treatment of benign prostatic hypertrophy. A typical dose for an adult human is about 161 mg per day of the mixture

IT 81403-80-7, Alfuzosin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. containing α1-blocker and Saw palmetto berry extract for treatment of benign prostatic hypertrophy)
RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)

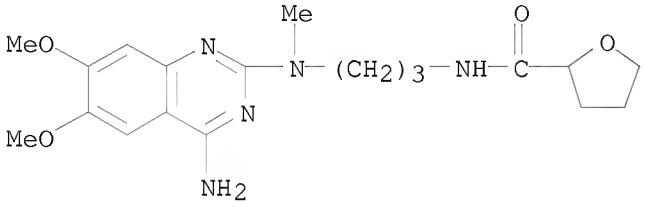


L5 ANSWER 36 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:719468 CAPLUS
DOCUMENT NUMBER: 136:11350
TITLE: Adsorptive voltammetric behavior of alfuzosin
AUTHOR(S): Cao, Erxin; Zeng, Yonghuai
CORPORATE SOURCE: Department of Chemistry, Beijing Normal University, Beijing, 100875, Peop. Rep. China
SOURCE: Zhongguo Yiyao Gongye Zazhi (2001), 32(8), 362-365
CODEN: ZYGZEA; ISSN: 1001-8255
PUBLISHER: Zhongguo Yiyao Gongye Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB The electrochem. behavior of alfuzosin (AFZ) was studied by linear-sweep polarog., cyclic voltammetry, and normal pulse polarog. In a supporting electrolyte containing 0.01M KH2PO4- K2HPO4 (pH 7.05), a reduction peak of AFZ was observed by linear-sweep voltammetry at Hg electrode. The peak showed adsorptive characteristics. The linear range for AFZ was (0.1-5.0) x 10-6M (γ = 0.999 2) with detection limit of 1.0 x 10-9M.

IT 81403-80-7, Alfuzosin
RL: ANT (Analyte); PRP (Properties); ANST (Analytical study)
(adsorptive voltammetric behavior of alfuzosin)
RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)

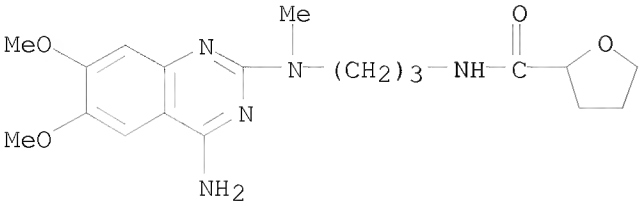


L5 ANSWER 37 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:719439 CAPLUS
DOCUMENT NUMBER: 136:401713
TITLE: Synthesis of Alfuzosin hydrochloride
AUTHOR(S): Zhang, Zhiyong
CORPORATE SOURCE: Team Academy of pharmaceutical Science, Beijing, 100071, Peop. Rep. China
SOURCE: Zhongguo Yiyao Gongye Zazhi (2001), 32(7), 289-291
CODEN: ZYGZEA; ISSN: 1001-8255
PUBLISHER: Zhongguo Yiyao Gongye Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
OTHER SOURCE(S): CASREACT 136:401713

AB Alfuzosin hydrochloride was synthesized from 3,4-dimethoxybenzoic acid via nitration, reduction, cyclization, chlorination, amination, condensation reaction with β-cyanoethylmethylamine, hydrogenation, amidation with 2-tetrahydrofuroic acid, and hydrochloride salt formation, giving the product with overall yield 7.2%.

IT 81403-68-1P, Alfuzosin hydrochloride
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of Afuzosin hydrochloride)
RN 81403-68-1 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro-, hydrochloride (1:1) (CA

INDEX NAME)



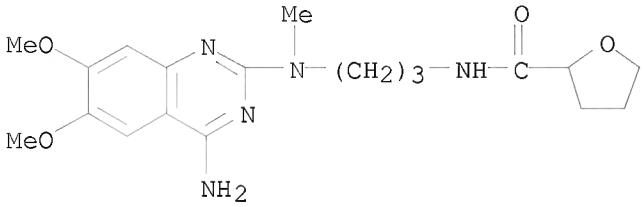
● HCl

L5 ANSWER 38 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:715670 CAPLUS
DOCUMENT NUMBER: 136:14937
TITLE: Efficacy and tolerability of drugs for treatment of benign prostatic hyperplasia
AUTHOR(S): Dutkiewics, S.
CORPORATE SOURCE: Department of Urology, Central Clinical Hospital, Health Administration of the Capital, Ministry of Internal Affairs, Warsaw, Pol.
SOURCE: International Urology and Nephrology (2000), 32(3), 423-432
CODEN: IURNAE; ISSN: 0301-1623
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. It has long been recognized that neural factors are of considerable importance in lower urinary tract function. While reduction in the bulk of the human prostate is feasible, experience on this therapeutic approach proved to be disappointing. Existing trial data with the agent finasteride are reviewed. A number of formulations derived from plant exts. have been advocated but their mechanism of action remain largely obscure and there is a dearth of placebo controlled information to support their efficacy. Experience over the last 10 yr has demonstrated efficacy with the use of alpha adrenoceptor blockade in the management of BPH. Alpha adrenoceptor antagonists relax the prostatic smooth muscle by interrupting the sympathetic pathway at the receptor level. Recent developments in this field include the recognition that there are alpha 1 adrenoceptor subtypes. The functional adrenoceptor in the human prostate is predominantly the alpha 1A - subtype. Of the alpha 1-adrenoceptor antagonists only tamsulosin discriminates between the alpha 1-adrenoceptor subtypes. Alpha 1-blockers should be used in first-line medical therapy for BPH and 5-alpha-reductase inhibitors reserved for those patients in whom alpha-blocker therapy fails. Alpha 1-blockers such as doxazosin, tamsulosin, terazosin, alfuzosin are effective in the treatment of BPH both in younger and in older men. The drugs are well tolerated. The majority of side effects were classified as minor and mild. The most common complaints, as with other alpha-blockers, are dizziness, fatigue and headache, and these are often transient. In contrast, finasteride can lead to impotence, reduced libido, gynecomastia or ejaculatory disorders. Men with small prostates may not be suitable candidates for finasteride therapy.

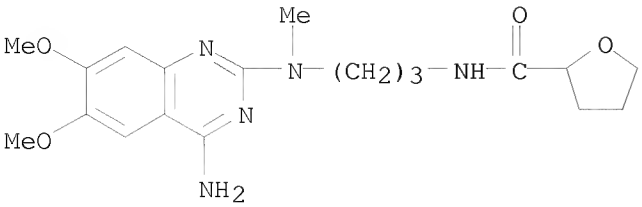
IT 81403-80-7, Alfuzosin
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of

action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(efficacy and tolerability of drugs for treatment of benign prostatic hyperplasia in humans)
RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 39 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:419865 CAPLUS
DOCUMENT NUMBER: 135:251701
TITLE: The efficacy and safety of a new once-a-day formulation of an α-blocker
AUTHOR(S): Van Kerrebroeck, Ph. E. V.
CORPORATE SOURCE: Department of Urology, University Hospital of Maastricht, Maastricht, Neth.
SOURCE: European Urology (2001), 39(Suppl. 6), 19-26
CODEN: EUURAV; ISSN: 0302-2838
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Aim of this study was to assess the long-term efficacy and safety of alfuzosin 10 mg OD in patients with symptomatic BPH. Patients (>50 yr) were randomized to alfuzosin 10 mg OD, alfuzosin 2.5. mg t.i.d. or placebo for 3 mo. Open-label alfuzosin 10 mg OD was continued for up to 1 yr. Efficacy assessments included the International Prostate Symptom Score (I-PSS) and quality of life index and uroflowmetry. At 3 mo, there was a significant reduction in I-PSS and a significant improvement in peak flow rate for both alfuzosin groups compared with placebo ($p < 0.05$). Vasodilatory adverse experiences were more common in the alfuzosin 2.5 mg group than the 10 mg OD group. Improvements in symptoms and flow rate with alfuzosin 10 mg OD were maintained for up to 12 mo. Alfuzosin 10 mg OD is an effective treatment for symptomatic BPH for at least 12 mo, with a better cardiovascular safety profile than the immediate release formulation.
IT 81403-80-7, Alfuzosin
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(new once-a-day formulation of an α-blocker alfuzosin in humans with symptomatic benign prostate hyperplasia (BPH))
RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



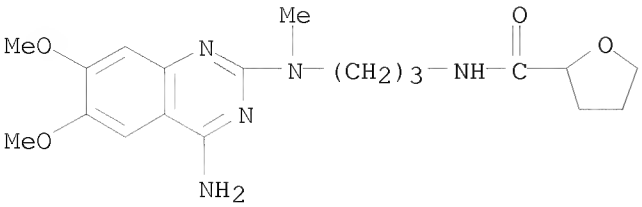
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 40 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:419864 CAPLUS
DOCUMENT NUMBER: 135:251274
TITLE: Do alpha-blockers prevent the occurrence of acute urinary retention?
AUTHOR(S): Hartung, R.
CORPORATE SOURCE: Department of Urology, Technical University of Munich, Munich, D-81676, Germany
SOURCE: European Urology (2001), 39(Suppl. 6), 13-18
CODEN: EUURAV; ISSN: 0302-2838
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 36 refs. Acute urinary retention (AUR) is a common complication of benign prostatic hyperplasia (BPH) and the incidence varies widely from 0.4 to 25% per yr in men seen in urol. practices. It has been estimated that AUR is the indication for surgery in around 25-30% of patients undergoing transurethral resection of the prostate (TURP) and that emergency TURP for AUR is associated with greater morbidity than elective TURP. Risk factors for AUR include lower urinary tract symptoms (LUTS), depressed peak urinary flow rate, enlarged prostate, high postvoid residual (PVR) urine and old age. Alfuzosin has been shown to significantly increase maximum flow rate and relieve bladder outlet obstruction, resulting in a reduction in PVR urine. A pooled anal. of 11 placebo-controlled studies involving 1,470 patients with LUTS suggestive of BPH indicates that significantly greater improvements were observed in patients treated with alfuzosin than with placebo. A 6-mo placebo controlled study of 518 patients reported a 0.4% incidence of AUR in the alfuzosin group compared with a 2.4% incidence with placebo (p = 0.04). These pos. effects on PVR could be related to the reduction in incidence of AUR seen in alfuzosin-treated patients.

IT 81403-80-7, Alfuzosin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alpha-blockers for prevention of acute urinary retention in humans with benign prostatic hyperplasia (BPH))

RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



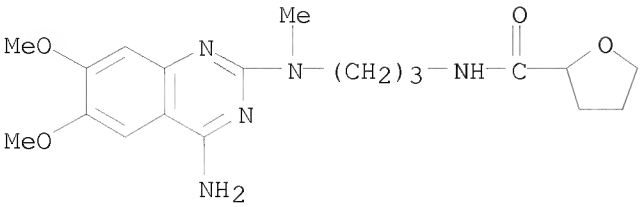
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 41 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:419863 CAPLUS
DOCUMENT NUMBER: 135:251273
TITLE: Does acute urinary retention respond to alpha-blockers alone?
AUTHOR(S): McNeill, S. A.
CORPORATE SOURCE: Western General Hospital, Edinburgh, EH4 2XU, UK
SOURCE: European Urology (2001), 39(Suppl. 6), 7-12
CODEN: EUURAV; ISSN: 0302-2838
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 22 refs. Studies show that men who undergo prostatectomy after acute urinary retention (AUR) are at increased risk of intraoperative complications, transfusions, postoperative complications and hospital death. Urethral catheterization for AUR has also been shown to result in bacterial colonization at a rate of 4% per day. Consequently, it is preferable that patients undergo a trial without catheter (TWOC) after an episode of AUR to potentially avoid surgery altogether, or to avoid having a urinary catheter in situ even if they do come to prostatectomy. A number of small studies indicate that α1 blockers may improve the success rate of a TWOC. A placebo-controlled TWOC study of alfuzosin in 81 patients with AUR shows that a successful TWOC was achieved in 55% of alfuzosin-treated patients compared with 29% in the placebo group (p = 0.03). Long-term follow-up suggest that 32% (11/34; 22 treated with alfuzosin and 12 with placebo) of the patients had a further episode of AUR at a mean of 4.1 mo following their first episode. This shows that there is a window of opportunity for surgical intervention prior to the occurrence of a second episode of AUR. Patients who had a subsequent episode of AUR or who needed surgery were found to have a higher post-void residual (PVR) urine following their successful TWOC, and thus may be identified as candidates for close follow-up and early intervention. As alfuzosin has been shown to reduce PVR, this factor may help prevent recurrent retention following TWOC.

IT 81403-80-7, Alfuzosin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alpha-blockers for acute urinary retention in humans with benign prostatic hyperplasia (BPH))

RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



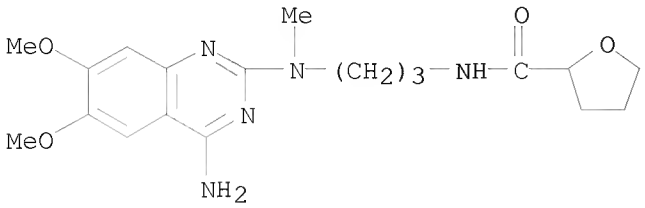
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 42 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:287568 CAPLUS
DOCUMENT NUMBER: 135:204704
TITLE: Lower urinary tract symptoms suggestive of benign prostatic obstruction - triumph: the role of general practice databases
AUTHOR(S): Logie, John W.; Clifford, Gary M.; Farmer, Richard D. T.; Meesen, Bianca P. W.
CORPORATE SOURCE: Department of Pharmacoepidemiology and Public Health, Postgraduate Medical School, University of Surrey, Guildford, GU2 7DJ, UK
SOURCE: European Urology (2001), 39(Suppl. 3), 42-47
CODEN: EUURAV; ISSN: 0302-2838
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 31 refs. The Triumph project aims to document the current management of lower urinary tract symptoms (LUTS) suggestive of benign prostatic hyperplasia (BPH) in general practice and to assess the effectiveness of the initial treatment options used. The first phase of the project will consider existing data sources in primary care. A patient's medical record will contain most, if not all, clin. relevant information, and databases combining the records from a network of computerized general practices can provide longitudinal data for complete populations, linking prescribing records to clin. information on disease progression and outcomes for individual patients. Database research can provide rapid information and offers the ability to conduct studies on a scale that would previously have been prohibited by both time and expense. Within the Triumph project, the THALES, General Practice Research Database (GPRD) and Integrated Primary Care Information (IPCI) databases are, or will be, used to examine the current management of LUTS/BPH in France, the UK and the Netherlands resp. Preliminary results from the UK General Practice Research Database (GPRD) showed that LUTS/BPH incidence increased linearly from the ages of 45 to 85 yr (r2 = 0.992) and prevalence increased from 3.5% to 35% for men in their late 40s and 80s resp. With treatment failure defined as a change to another medical therapy, catheterization or prostatic surgery, and accounting for age and year variation, patients receiving the older α1-blockers (indoramin and prazosin) appeared to fail significantly earlier than those receiving finasteride. There was no significant difference between finasteride and the newer α1-blockers (tamsulosin, alfuzosin, terazosin and doxazosin). Patterns of changes between products from the THALES database in France were broadly similar to those seen in the UK.

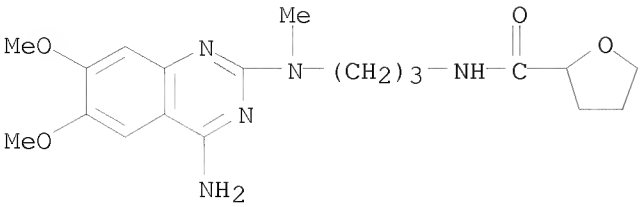
IT 81403-80-7, Alfuzosin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(treatment of benign prostatic obstruction in men)
RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 43 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:255748 CAPLUS
DOCUMENT NUMBER: 135:189565
TITLE: Role of alpha-blockers in the treatment of BPH
AUTHOR(S): Montorsi, F.; Salonia, A.; Fabris, G. F. Menchini; Rigatti, P.
CORPORATE SOURCE: Divisione di Urologia, IRCCS Ospedale San Raffaele, Milan, Italy
SOURCE: International Congress on Therapy in Andrology: The Human Testis: Its Role in Reproduction and Sexuality, 4th, Pisa, Italy, Oct. 14-16, 1999 (1999), 181-185. Editor(s): Menchini Fabris, G. F. Monduzzi Editore S.p.A.: Bologna, Italy.
CODEN: 69BDFM
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review with 17 refs. Therapeutic innovations provide a range of available and future options to prevent the necessity for surgical resolution of the problem. Because the dynamic obstruction of the bladder outlet secondary to BPH and the contractile properties of the human prostate are mediated primarily by α1-adrenoceptors, selective α-adrenergic antagonists (prazosin, terazosin, doxazosin, alfuzosin and tamsulosin) have been developed in the urol. field. Data derived from more than 7000 patients indicated that all alpha-1 blockers produce comparable results in subjective symptoms and urinary flow. Alfuzosin and tamsulosin seem to be better tolerated than terazosin and doxazosin.
IT 81403-80-7, Alfuzosin
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alpha-blockers in treatment of BPH in humans)
RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 44 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:228701 CAPLUS
DOCUMENT NUMBER: 134:247264
TITLE: Treatment of lower urinary tract symptoms with muscarinic and α-adrenergic antagonists and 5α-reductase inhibitors, and pharmaceutical compositions for use therein
INVENTOR(S): Stoner, Elizabeth; Drake, Paul J.; Bach, Mark A.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001021167	A1	20010329	WO 2000-US25534	20000918

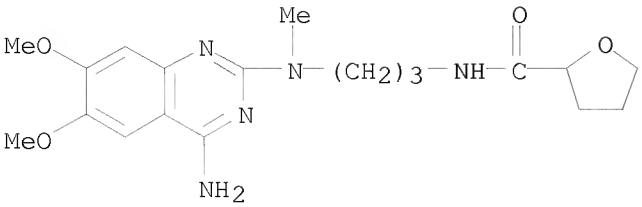
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-155357P P 19990922
OTHER SOURCE(S): MARPAT 134:247264

AB A medical condition in men known as Lower Urinary Tract Symptoms (LUTS) is treated by the administration of a muscarinic receptor antagonist in combination with at least one of a 5α-reductase inhibitor and an α-adrenergic receptor blocker.

IT 81403-80-7, Alfuzosin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(muscarinic and α-adrenergic antagonists and 5α-reductase inhibitors for treatment of lower urinary tract symptoms, and pharmaceutical compns.)

RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

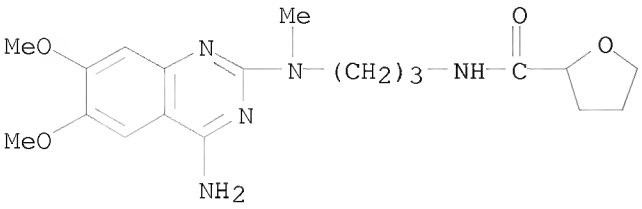
L5 ANSWER 45 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:20811 CAPLUS
DOCUMENT NUMBER: 134:320749
TITLE: A quantitative analysis of antagonism and inverse agonism at wild-type and constitutively active hamster α1B-adrenoceptors
AUTHOR(S): Hein, Peter; Goepel, Mark; Cotecchia, Susanna; Michel, Martin C.
CORPORATE SOURCE: Nephrol. Lab. IG 1, Klinikum Essen, Essen, 45122, Germany
SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology (2001), 363(1), 34-39
CODEN: NSAPCC; ISSN: 0028-1298
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In order to characterize inverse agonism at α1B-adrenoceptors, we have compared the concentration-response relationships of several quinazoline and non-quinazoline α1-adrenoceptor antagonists at cloned hamster wild-type (WT) α1B-adrenoceptors and a constitutively active mutant (CAM) thereof upon stable expression in Rat-1 fibroblasts. Receptor activation or inhibition thereof was assessed as [3H]inositol phosphate (IP) accumulation. Quinazoline (alfuzosin, doxazosin, prazosin, terazosin) and non-quinazoline α1-adrenoceptor antagonists (BE 2254, SB 216,469, tamsulosin) concentration-dependently inhibited phenylephrine-stimulated IP formation at both WT and CAM with Ki values similar to those previously found in radioligand binding studies. At CAM in the absence of phenylephrine, the quinazolines produced concentration-dependent inhibition of basal IP formation; the maximum inhibition was .apprx.55%, and the corresponding EC50 values were slightly smaller than the Ki values. In contrast, BE 2254 produced much less inhibition of basal IP formation, SB 216,469 was close to being a neutral antagonist, and tamsulosin even weakly stimulated IP formation. The inhibitory effects of the quinazolines and BE 2254 as well as the stimulatory effect of tamsulosin were equally blocked by SB 216,469 at CAM. At WT in the absence of phenylephrine, tamsulosin did not cause significant stimulation and none of the other compds. caused significant inhibition of basal IP formation. We conclude that α1-adrenoceptor antagonists with a quinazoline structure exhibit greater efficacy as inverse agonists than those without.

IT 81403-80-7, Alfuzosin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(a quant. anal. of antagonism and inverse agonism at wild-type and constitutively active hamster α1B-adrenoceptors)

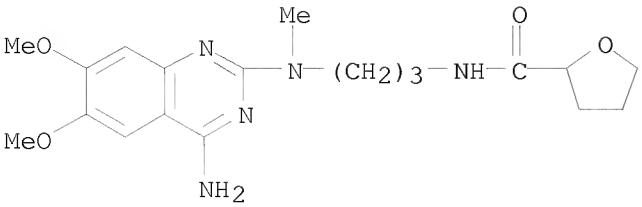
RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-

quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



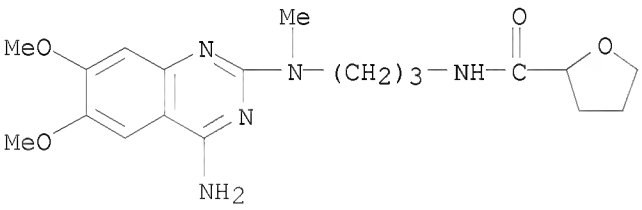
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 46 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:11729 CAPLUS
DOCUMENT NUMBER: 135:102201
TITLE: α-blockade improves symptoms suggestive of bladder outlet obstruction but fails to relieve it
AUTHOR(S): Rossi, Cristina; Kortmann, Barbara B. M.; Sonke, Gabe S.; Floratos, Diamandis L.; Kiemeney, Lambertus A. L. M.; Wijkstra, Hessel; De La Rosette, Jean J. M. C. H.
CORPORATE SOURCE: Department of Urology, University Medical Centre Nijmegen, Nijmegen, Neth.
SOURCE: Journal of Urology (Baltimore) (2001), 165(1), 38-41
CODEN: JOURAA; ISSN: 0022-5347
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We investigated the effect of the α-blockers alfuzosin, terazosin and tamsulosin on urodynamic parameters after 6 mo of therapy. Between Feb. 1992 and June 1998, 163 patients with lower urinary tract symptoms suggestive of bladder outlet obstruction were treated with alfuzosin (60), terazosin (66) and tamsulosin (37). Patients were evaluated with urodynamic studies, including pressure flow anal., before treatment and after 6 mo of therapy. Initially, all patients were also assessed by the International Prostate Symptom Score questionnaire and measurement of urinary flow rate. The majority of patients had no clear improvement in obstructive parameters, regardless of the α-blocker used, as urethral resistance factor and detrusor pressure maximum flow rate decreased by only 4 cm. H2O. There was a clear subjective and statistically significant decrease in International Prostate Symptom Score and quality of life scores of 6 and 2 points, resp. No relevant statistical difference was noted among the effects of the 3 α-blockers on relieving symptoms or improving urodynamic parameters of obstruction. The α-blockers are effective for treating symptoms suggestive of bladder outlet obstruction in patients presenting with lower urinary tract symptoms but not for treating the obstruction.
IT 81403-80-7, Alfuzosin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of α-blockers alfuzosin, terazosin and tamsulosin on urodynamic parameters in humans with suggestive of bladder outlet obstruction)
RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 47 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:840364 CAPLUS
DOCUMENT NUMBER: 134:320430
TITLE: Benign prostatic obstruction complications and need for surgery
AUTHOR(S): Michel, M. C.
CORPORATE SOURCE: University of Essen Medical School, Essen, Germany
SOURCE: Drugs of Today (2000), 36(Suppl. F), 11-13
CODEN: MDACAP; ISSN: 0025-7656
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 6 refs., focusing on the effects of medical therapy on the development of acute urinary retention and on the progression to surgery.
IT 81403-80-7, Alfuzosin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of benign prostatic obstruction complications with α1-adrenoceptor antagonists and finasteride in relation to surgery)
RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

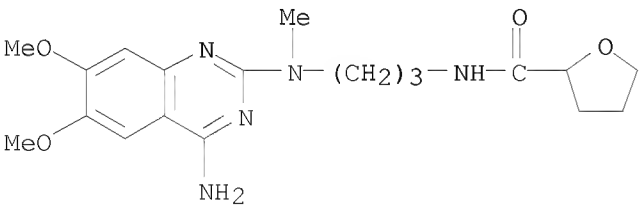
L5 ANSWER 48 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:716814 CAPLUS
DOCUMENT NUMBER: 134:261056
TITLE: The clinical uroselectivity of alfuzosin is not significantly affected by the age of patients with lower urinary tract symptoms suggestive of benign prostatic hyperplasia
AUTHOR(S): Sanchez-Chapado, M.; Guil, M.; Badiella, L. I.; Fernandez-Hernando, N.; Alfaro, V.

CORPORATE SOURCE: Urology Service, Hospital Universitario Principe de Asturias, Alcala de Henares, Madrid, Spain
SOURCE: BJU International (2000), 86(4), 432-438
CODEN: BJINFO; ISSN: 1464-4096
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Objective: To assess the effect of the age of patients with benign prostatic hyperplasia (BPH) on the clin. uroselectivity of alfuzosin during general medical practice. Patients and methods: The present national, multicenter, open-labeled, observational study involved 4018 Spanish outpatients with BPH, i.e. showing lower urinary tract symptoms (LUTS) suggestive of benign prostatic obstruction. The patients received sustained release (SR) alfuzosin, 5 mg twice daily, for 2 mo. The primary efficacy criteria were symptomatic improvements, as assessed by the International Prostate Symptom Score (IPSS) and quality of life (QoL) index. Safety was assessed by monitoring cardiovascular data and adverse events. Results: The patients were divided into four age groups, i.e. < 56, 56-65, 66-75 and > 75 yr. All groups of patients showed a mean IPSS decrease of 11-12 (55.8-65.4% from baseline) at the end of the study, while the QoL decreased by 2-3 points (55.6-63.6% from baseline). There were no relevant effects of age on the efficacy of the treatment. Moreover, alfuzosin was well tolerated independently of the age of the patient; 1.2% of the patients enrolled withdrew because of adverse events. The qual. distribution of vasodilatory/nonvasodilatory adverse events was similar in all age groups. The incidence of asymptomatic orthostatic hypotension was low (0.58%) and not affected by the age of the patients. Conclusion: This study confirms that the clin. uroselectivity of SR-alfuzosin, already described in randomized controlled studies, is not significantly affected in clin. practice by the age of the patients. This is considered particularly relevant to the characteristics of patients with BPH, as they are mostly elderly men.

IT 81403-80-7, Alfuzosin
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alfuzosin therapy in elderly humans with lower urinary tract symptoms suggestive of benign prostatic hyperplasia)

RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

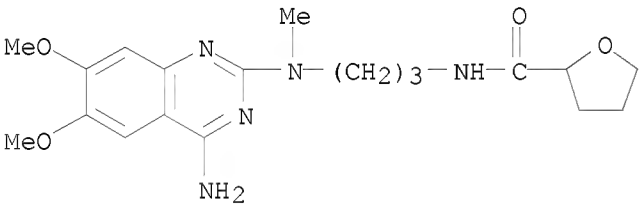
L5 ANSWER 49 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:606289 CAPLUS
DOCUMENT NUMBER: 134:154
TITLE: Bioavailability of alfuzosin hydrochloride from tablets in healthy subjects

AUTHOR(S): Li, Yang; Wang, Wei; Wang, Ru-Wei; Liu, Lei; Shi, Ai-Xin; He, Guang-Wei; Li, Ke-Xin; Sun, Cun-Hua; Song, You-Hua
CORPORATE SOURCE: Clinical Pharmacy Base, Beijing Hospital, Beijing, 100730, Peop. Rep. China
SOURCE: Zhongguo Linchuang Yaolixue Zazhi (2000), 16(2), 129-131
CODEN: ZLYZE9; ISSN: 1001-6821
PUBLISHER: Beijing Yike Daxue, Linchuang Yaoli Yanjiuso
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB The relative bioavailability and pharmacokinetics of alfuzosin-HCl from Chinese-manufactured (domestic) vs. reference (imported) tablets were studied in healthy male volunteers. A dose of 5 mg alfuzosin-HCl in domestic or imported tablets was given according to a randomized 2-way cross-over design. Plasma concns. of alfuzosin were determined by HPLC. The concentration-time curves of the prepns. were fitted to a 2-compartment model. The peak plasma levels of alfuzosin following administration of the domestic and imported tablets were 39.79 and 40.05 μg/L, resp., the peak times were 1.46 and 1.42 h, resp., and the AUC0-24h values were 225.40 and 235.04 μg/h/L, resp. The pharmacokinetic and relative bioavailability data proved the bioequivalence of the domestic and imported alfuzosin-HCl tablets.

IT 81403-80-7, Alfuzosin
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(bioavailability and pharmacokinetics of alfuzosin hydrochloride from tablets in humans)

RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



L5 ANSWER 50 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:602380 CAPLUS
DOCUMENT NUMBER: 133:171695
TITLE: HPLC for plasma concentration of alfuzosin hydrochloride
AUTHOR(S): Li, Yang; Li, Kexin; Wang, Wei; Liu, Lei; Shi, Aixin; Hao, Guangwei; Sun, Chunhua
CORPORATE SOURCE: Clinical Pharmacology, Beijing Hospital, Beijing, 100730, Peop. Rep. China
SOURCE: Zhongguo Yiyuan Yaoxue Zazhi (2000), 20(6), 344-346
CODEN: ZYYAEP; ISSN: 1001-5213
PUBLISHER: Zhongguo Yiyuan Yaoxue Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

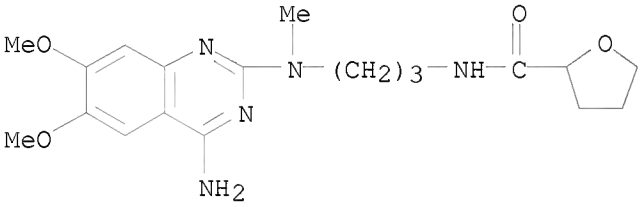
AB The plasma concentration of alfuzosin was determined by HPLC on a LUNA C18 column with

MeCN-pH 2.5 0.02M potassium dihydrogen phosphate as mobile phase. The linear range was 0.781 3-50 μg L-1 with detection limit of 0.7 μg L-1. The average recovery was 98.9%. The coefficient variation of within and between-day for the concentration of 50, 20, and 1,5 μg L-1 was 3.74, 4.72, 5.68 and 6.00, 9.43, 10.27%, resp. The method may be used for determining plasma concentration of alfuzosin.

IT 81403-80-7, Alfuzosin
RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(HPLC for determination of alfuzosin in blood plasma)

RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



L5 ANSWER 51 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:592530 CAPLUS

DOCUMENT NUMBER: 133:183005

TITLE: Pharmaceutical composition for balanic transmucosal administration of alfuzosin

INVENTOR(S): Charlier, Anne; Cuine, Alain; Dufour, Alain

PATENT ASSIGNEE(S): Sanofi-Synthelabo, Fr.

SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

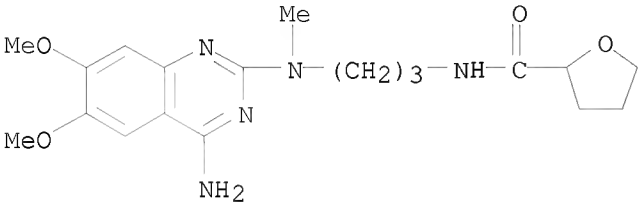
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000048570	A1	20000824	WO 2000-FR358	20000214
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2789586	A1	20000818	FR 1999-1803	19990216
PRIORITY APPLN. INFO.:			FR 1999-1803 A	19990216

AB The invention concerns a pharmaceutical composition for balanic transmucosal administration, characterized in that it comprises an active principle consisting in alfuzosin, in free form or one of its salts, and an exclusively hydrophile or partly hydrophile absorption promoter. A topical gel contained alfuzosin hydrochloride 4, Soketal 10, Miglyol 15, Poloxamer 407 15, isopropanol 5, and water q.s. 100%.

IT 81403-68-1, Alfuzosin hydrochloride 81403-80-7,

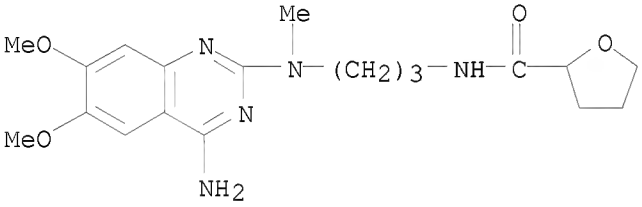
Alfuzosin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical composition for balanic transmucosal administration of alfuzosin)

RN 81403-68-1 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 52 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:531583 CAPLUS
DOCUMENT NUMBER: 133:140256
TITLE: Controlled release pharmaceutical dosage forms containing polymers
INVENTOR(S): Ayer, Atul D.; Lam, Andrew; Magruder, Judy A.; Hamel, Lawrence G.; Wong, Patrick S. L.
PATENT ASSIGNEE(S): Alza Corporation, USA
SOURCE: U.S., 15 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6096339	A	20000801	US 1997-826642	19970404
US 6534089	B1	20030318	US 2000-602916	20000623
US 20020114838	A1	20020822	US 2001-5594	20011107

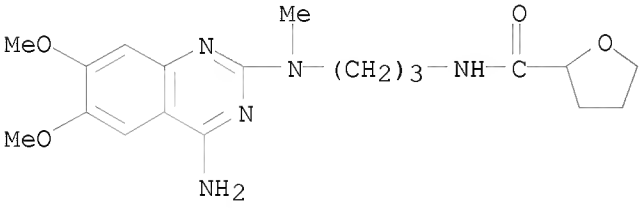
PRIORITY APPLN. INFO.: US 1996-14889P P 19960405
US 1997-826642 A1 19970404
US 2000-602916 B1 20000623

AB The invention disclosed pertains to a controlled-release dosage form comprising a drug and a pharmaceutical carrier (a hydrophilic polymer) of the right particle size. The drug has a particle size of <150 μm and the polymer has the size <250 μm.

IT 81403-80-7, Alfuzosin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlled release pharmaceutical dosage forms containing polymers)

RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 53 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:509793 CAPLUS

DOCUMENT NUMBER: 133:246867

TITLE: Safety, efficacy and impact on patients' quality of life of a long-term treatment with the α1-blocker alfuzosin in symptomatic patients with BPH

CORPORATE SOURCE: The Italian Alfuzosin Co-Operative Group, Department of Urology, Sant "Anna" Hospital, Como, I-22100, Italy

SOURCE: European Urology (2000), 37(6), 680-686
CODEN: EUURAV; ISSN: 0302-2838

PUBLISHER: S. Karger AG

DOCUMENT TYPE: Journal

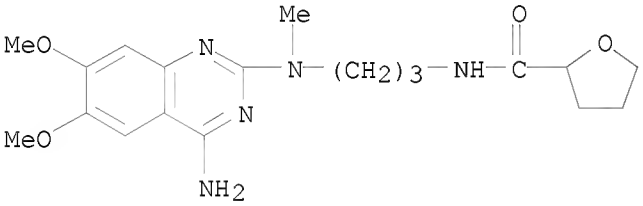
LANGUAGE: English

AB The aim of this study was to assess the impact of a 12-mo treatment period with alfuzosin, 2.5 mg t.i.d, on symptomatic patients with BPH (n = 355) by means of the International Prostate Symptom Score (I-PSS), the Symptom Problem Index (SPI), the BPH Impact Index (BII), and the single Quality of Life (QoL) question proposed by the WHO. This was a naturalistic study, carried out under conditions of normal practice by 22 centers of urol. At baseline and on a quarterly basis up to 12 mo of treatment, subjective and objective (uroflowmetry and residual urine volume) responses of the patients were evaluated. The appearance of adverse medical events (AMEs) was carefully monitored and recorded throughout the trial. Both the BII and the Qol question improved gradually over time (60 and 54.6%, resp., after 12 mo of treatment). At any visits, the improvements were statistically significant vs. the baseline ($p<0.01$). Alfuzosin was able to improve the BPH symptoms progressively and significantly over time: total mean score I-PSS: 3rd month = 22.7%, 6th month = 38.4%, 9th month 0.50%, 12th month = 61.6%. The improvement was more marked in patients with severe symptoms at baseline (I-PSS score 20-35, 63.6%). A progressive and marked improvement over time of the problems due to symptoms (SPI) was observed in the whole population (61.7% after 12 mo of treatment). After 12 mo of

treatment, uroflowmetric data showed a significant increase in peak (+5.5 mL/s) flow rate, associated with a marked decrease in residual volume: -31 mL (-53.5%). Twenty-five patients (7.1%) experienced one or more AMEs (total AMEs n = 44). Globally, 14 vasodilatory events and 30 non-vasodilatory events were reported. Fifteen (4.3%) patients dropped out prematurely from the study for safety reasons. Seven serious AMEs were reported during the study period. This study showed that long-term treatment with alfuzosin in usual clin. practice had a continued and pos. impact on the patients' QoL.

IT 81403-80-7, Alfuzosin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(safety, efficacy and impact on patients' quality of life of a long-term treatment with the α1-blocker alfuzosin in symptomatic patients with benign prostate hyperplasia)

RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

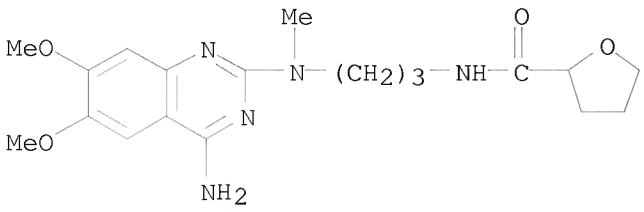
L5 ANSWER 54 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:503848 CAPLUS
DOCUMENT NUMBER: 133:89492
TITLE: Chiral separation of three new antagonists of α-1-adrenoceptors by capillary electrophoresis
AUTHOR(S): Niu, Changqun; Ren, Leiming
CORPORATE SOURCE: Department of Pharmacology, School of Pharmacy, Hebei Medical University, Shijiazhuang, 050017, Peop. Rep. China
SOURCE: Yaoxue Xuebao (2000), 35(6), 451-453
CODEN: YHHPAL; ISSN: 0513-4870
PUBLISHER: Yaoxue Xuebao Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB The title antagonists (alfuzosin, terazosin, and doxazosin) were separated by capillary electrophoresis. The effects of the kinds and concns. of cyclodextrin, the pH value, and the concentration of buffer on chiral separation were studied, and the optimum conditions for chiral separation were presented. The enantiomers of three new drugs were separated at baseline. The results showed that the chiral separation method can be used to study the enantiomers of three new drugs.

IT 81403-80-7P, Alfuzosin
RL: ANT (Analyte); PNU (Preparation, unclassified); ANST (Analytical study); PREP (Preparation)
(chiral separation of quinazoline derivs. by capillary electrophoresis)

RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



L5 ANSWER 55 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:263451 CAPLUS
DOCUMENT NUMBER: 132:274259
TITLE: Efficacy and safety of a new prolonged release formulation of alfuzosin 10 mg once daily versus alfuzosin 2.5 mg thrice daily and placebo in patients with symptomatic benign prostatic hyperplasia
AUTHOR(S): Van Kerrebroeck, P.; Jardin, A.; Laval, K. U.; Van Cangh, P.
CORPORATE SOURCE: ALFORTI Study Group, Department of Urology, Academisch Ziekenhuis, Maastricht, NL-6202 AZ, Neth.
SOURCE: European Urology (2000), 37(3), 306-313
CODEN: EUURAV; ISSN: 0302-2838
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English

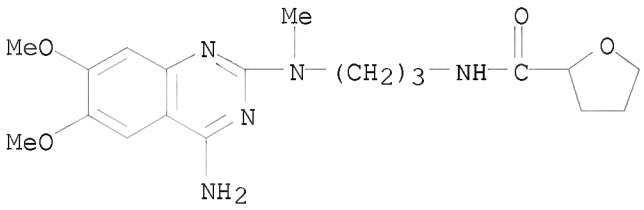
AB Objectives: To assess the efficacy and safety of a new prolonged release formulation of the uroselective α1-blocker alfuzosin for a once-daily dosing regimen in patients with lower urinary tract symptoms (LUTS) suggestive of symptomatic benign prostatic hyperplasia (BPH). Methods: After a 1-mo run-in period, 447 patients were randomly allocated in a double-blind placebo-controlled study to receive alfuzosin 10 mg once daily (n = 143), alfuzosin 2.5 mg thrice daily (n = 150) or placebo (n = 154) for 3 mo. At inclusion, 46% of the randomized population had concomitant cardiovascular disease and 30% received an antihypertensive treatment. Uroflowmetry was performed close to trough plasma concentration of alfuzosin once daily to demonstrate the 24-h coverage with this formulation. Results: Both alfuzosin formulations significantly improved urinary symptoms vs. placebo assessed using the International Prostate Symptom Score (alfuzosin 10 mg once daily: -6.9; alfuzosin 2.5 mg thrice daily: -6.4; placebo: -4.9, p = 0.005). Peak flow rate increased significantly with alfuzosin 10 mg once daily (+2.3 mL/s, p = 0.03 vs. placebo) and with alfuzosin 2.5 mg thrice daily (+3.2 mL/s, p<0.0001 vs. placebo) compared to placebo (+1.4 mL/s). Overall both formulations of alfuzosin were well tolerated in comparison with placebo. In addition, vasodilatory adverse events appeared to be less frequent with the once daily than the thrice daily formulation (6.3 vs. 9.4%, resp.). No first-day effect was reported with alfuzosin once daily and the effect on blood pressure did not differ from those observed in placebo, both in normotensive and hypertensive patients. No specific sexual dysfunction including ejaculation disorder was reported in the alfuzosin 10 mg once-daily group. Conclusion: The new once-daily formulation of alfuzosin administered at a dose of 10 mg daily is an effective 24-h treatment of LUTS associated with BPH. Alfuzosin is as effective as the immediate formulation and shows a better cardiovascular safety. The better safety profile enables the same dose to be used in all patients, providing the

patients with the benefits of a once-daily administration.

IT 81403-80-7, Alfuzosin
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(efficacy and safety of new prolonged release alfuzosin formulation in humans with symptomatic benign prostatic hyperplasia)

RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 56 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:263329 CAPLUS

DOCUMENT NUMBER: 132:274300

TITLE: Safety and efficacy of sustained-release alfuzosin on lower urinary tract symptoms suggestive of benign prostatic hyperplasia in 3,095 spanish patients evaluated during general practice

AUTHOR(S): Sanchez-Chapado, M.; Guil, M.; Alfaro, V.; Badiella, Ll.; Fernandez-Hernando, N.

CORPORATE SOURCE: Urology Service, Hospital Universitario Principe de Asturias, Alcala de Henares, Madrid, Spain

SOURCE: European Urology (2000), 37(4), 421-427
CODEN: EUURAV; ISSN: 0302-2838

PUBLISHER: S. Karger AG

DOCUMENT TYPE: Journal

LANGUAGE: English

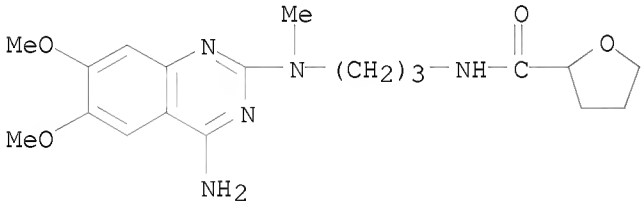
AB Objectives: This general practitioner-run study assess the security as well as the efficacy and impact on health-related quality of life of a sustained-release (SR) form of alfuzosin in Spanish patients suffering from lower urinary tract symptoms (LUTS) suggestive of benign prostatic hyperplasia (BPH). Material and Methods: 3,095 patients with symptomatic BPH were enrolled into a national, multicentric, open, phase IV observational study. The period of active treatment studied (5 mg, twice daily) was 60 days. Safety was assessed by monitoring blood pressure and spontaneous adverse events. Symptoms were assessed using a validated Spanish International Prostate Symptom Score (I-PSS). Impact of symptoms on health-related quality of life was assessed using the quality of life index (L). Results: 101 adverse events were reported in 82 patients (2.6%). 28 adverse events (2.6%) were classified as severe. 49 patients (1.6%) dropped out of the study due to adverse events but only 17 of these patients (0.5%) showed adverse events related to vasodilation. Incidence of postural events (vertigo, postural hypotension/hypotension, headache and dizziness) was low (55 patients, 1.8%) and effects on sexual function were found not significant: no retrograde ejaculation was reported and only 1 patient (0.03%) showed impotence. Blood pressure or heart rate showed no clin. significant changes. All the I-PSS scores decreased

significantly during the treatment with alfuzosin, improvement being excellent in 60% of the patients. Symptomatic improvement was associated with a significant improvement in health-related quality of life. Conclusions: This large study conducted during general practice on Spanish BPH patients confirms the efficacy on LUTS and good safety profile of SR alfuzosin, especially its low incidence of postural symptoms and no deleterious effect on sexual function.

IT 81403-80-7, Alfuzosin
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(safety and efficacy of sustained-release alfuzosin on lower urinary tract symptoms suggestive of benign prostatic hyperplasia in humans evaluated during general practice)

RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 57 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:218248 CAPLUS

DOCUMENT NUMBER: 132:231631

TITLE: History of 7,093 patients with lower urinary tract symptoms related to benign prostatic hyperplasia treated with alfuzosin in general practice up to 3 years

AUTHOR(S): Lukacs, B.; Grange, J. C.; Comet, D.; McCarthy, C.

CORPORATE SOURCE: Urology Department, Tenon Hospital, Paris, F-75970, Fr.

SOURCE: European Urology (2000), 37(2), 183-190
CODEN: EUURAV; ISSN: 0302-2838

PUBLISHER: S. Karger AG

DOCUMENT TYPE: Journal

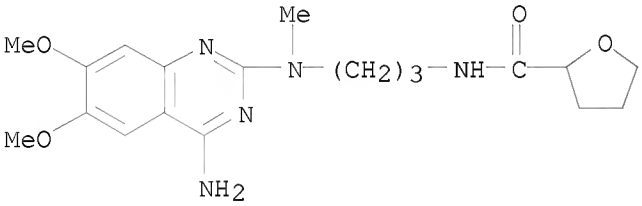
LANGUAGE: English

AB As we have previously published 4 articles reporting the treatment of 7,093 clin. benign prostatic hyperplasia (BPH) patients treated with alfuzosin in a 3-mo open-labeled study which was subsequently extended to 12, 24, and 36 mo, the objective of this article is to provide addnl. data on dropouts, acute urinary retention (AUR), progression to surgery, and safety under the natural conditions of general practice, paying special attention to the predictive factors. Seven thousand ninety-three patients were initially enrolled by 1,812 centers for up to 3 mo. Subsequently 1,508, 1,325, and 812 general practitioners agreed to extend the study up to 12, 24, and 36 mo, resp., which corresponds to 4 patient populations. The baseline symptom profile of patients who completed the study was identical to that of patients who dropped out (because the center resigned or during treatment). In the 4 patient populations, the percentage of patients per mo who dropped out, experienced adverse effects, AUR and

surgery were 0.6-1.6, 0.1-0.5, 0.01-0.03, and 0.1-0.3%, resp. The classes of symptom severity were not predictive for dropouts: 3.5, 12.6, 20, and 14.3% of the severe patients dropped out during treatment vs. 4.2, 13.7, 22.9, and 14.0% of the moderate patients who dropped out up to 3, 12, 24, and 36 mo, resp. Safety was satisfactory regarding the number of adverse events and blood pressure measurement. No retrograde ejaculation was reported. Under the natural conditions of general practice the reasons for dropping out were not correlated with symptom severity.

IT 81403-80-7, Alfuzosin
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(history of patients with lower urinary tract symptoms related to benign prostatic hyperplasia treated with alfuzosin)

RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 58 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:161149 CAPLUS
DOCUMENT NUMBER: 132:203141
TITLE: Anti-pressor agents and methods for remodeling neuronal and cardiovascular pathways for the long term management of sexual dysfunction
INVENTOR(S): Adams, Michael A.; Heaton, Jeremy P. W.
PATENT ASSIGNEE(S): Queen's University At Kingston, Can.
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

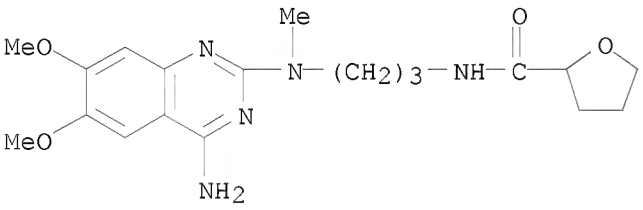
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000012110	A2	20000309	WO 1999-CA787	19990825
WO 2000012110	A3	20000803		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2340206	A1	20000309	CA 1999-2340206	19990825

AU 9954034 A1 20000321 AU 1999-54034 19990825
EP 1235563 A2 20020904 EP 1999-939874 19990825
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL
PRIORITY APPLN. INFO.: US 1998-98178P P 19980826
WO 1999-CA787 W 19990825

AB The invention provides a method of administration of an agent which acts to remodel neuronal or vascular pathways for the long term management of sexual dysfunction in both males and females. In a preferred embodiment, the invention provides a method of ameliorating or reversing pathogenic vascular degradative modeling in the ilio-hypogastric-pudendal arterial bed and genitalia comprising administering to a human patient in need of such treatment a therapeutically effective amount of an anti-pressor agent. The anti-pressor agent comprises one or more compds. selected from the therapeutic classes of direct vasodilators such as hydralazine and NO donors, ACE inhibitors, angiotensin-II receptor antagonists, α1-adrenergic receptor antagonists, β-adrenergic receptor antagonists, calcium channel blockers, and phosphodiesterase inhibitors. The anti-pressor agent may be co-administered with a diuretic compound, and is administered either chronically at low dose, or for short periods of time at doses higher than are typically used for the treatment of hypertension. In certain embodiments of the method of the invention, the anti-pressor agent is co-administered with a diuretic agent and/or prostaglandin-E1.

IT 81403-80-7, Alfuzosin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-pressor agents and methods for remodeling neuronal and cardiovascular pathways for long term management of sexual dysfunction)

RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



L5 ANSWER 59 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:125868 CAPLUS
DOCUMENT NUMBER: 132:245855
TITLE: Ligand design for α1-adrenoceptor subtype selective antagonists
AUTHOR(S): Bremner, John B.; Coban, Burak; Griffith, Renate; Groenewoud, Karina M.; Yates, Brian F.
CORPORATE SOURCE: Department of Chemistry, University of Wollongong, Wollongong, 2522, Australia
SOURCE: Bioorganic & Medicinal Chemistry (2000), 8(1), 201-214
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

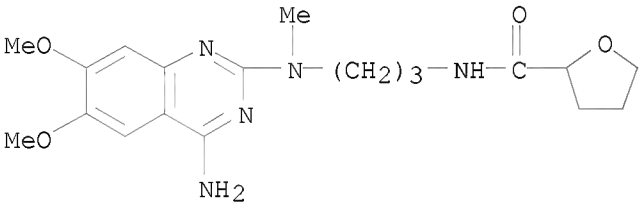
AB α1-Adrenoceptors have three subtypes and drugs interacting

selectively with these subtypes could be useful in the treatment of a variety of diseases. In order to gain an insight into the structural principles governing subtype selectivity, ligand based drug design (pharmacophore development) methods have been used to design a novel 1,2,3-thiadiazole ring D analog of the aporphine system. Synthesis and testing of this compound as a ligand on cloned and expressed human α1-adrenoceptors is described. Low binding affinity was found, possibly due to an unfavorable electrostatic potential distribution. Pharmacophore models for antagonists at the three adrenoceptor sites (α1A, α1B, α1D) were generated from a number of different training sets and their value for the design of new selective antagonists discussed. The first preliminary antagonist pharmacophore model for the α1D adrenoceptor subtype is also reported.

IT 81403-80-7, Alfuzosin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(ligand design for α1-adrenoceptor subtype selective antagonists)

RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 60 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:98335 CAPLUS

DOCUMENT NUMBER: 132:117559

TITLE: Use of alfuzosin for the manufacture of drugs intended for the treatment of disorders induced by smooth muscle contraction in the urinary tract, excluding contraction of α-adrenergic origin

INVENTOR(S): Eckert, Ralph

PATENT ASSIGNEE(S): Sanofi-Synthelabo, Fr.

SOURCE: PCT Int. Appl., 14 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000006168	A1	20000210	WO 1999-EP5278	19990723

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,

ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9951637 A1 20000221 AU 1999-51637 19990723

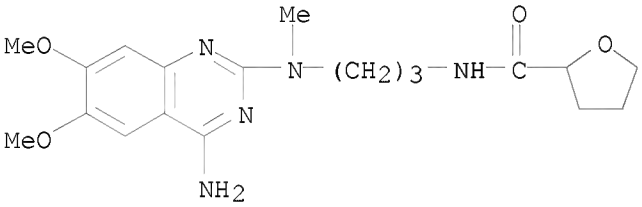
PRIORITY APPLN. INFO.: EP 1998-401917 A 19980728
WO 1999-EP5278 W 19990723

AB Alfuzosin and its pharmaceutically acceptable salts are used for manufacturing drugs intended for the treatment of disorders induced by smooth muscle contraction in the urinary tract, excluding contraction of α-adrenergic origin.

IT 81403-80-7, Alfuzosin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alfuzosin for treatment of disorders induced by urinary tract smooth muscle contraction, excluding contraction of α-adrenergic origin)

RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 61 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:9434 CAPLUS

DOCUMENT NUMBER: 132:146156

TITLE: Relevance of theoretical molecular descriptors in quantitative structure-activity relationship analysis of α1-adrenergic receptor antagonists

AUTHOR(S): Menziani, M. C.; Montorsi, M.; De Benedetti, P. G.; Karelson, M.

CORPORATE SOURCE: Department of Chemistry, University of Modena and Reggio Emilia, Modena, 41100, Italy

SOURCE: Bioorganic & Medicinal Chemistry (1999), 7(11), 2437-2451
CODEN: BMECEP; ISSN: 0968-0896

PUBLISHER: Elsevier Science Ltd.

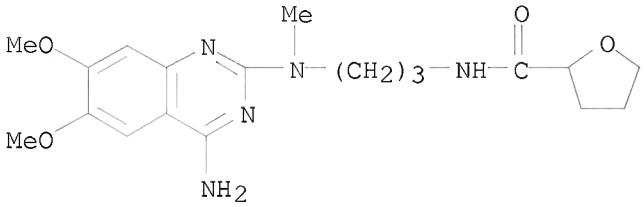
DOCUMENT TYPE: Journal

LANGUAGE: English

AB A quant. structure-activity relationship (QSAR) study of a wide series of structurally diverse α1-adrenergic receptor antagonists was performed using the CODESSA (Comprehensive Descriptors for Structural and Statistical Anal.) technique. Theor. descriptors derived on a single structure and ad hoc defined size and shape descriptors were considered in the attempt of describing information relevant to receptor interaction. The relative effectiveness of these two classes of parameters in developing QSAR models for native (α1A and α1B) and cloned (α1a, α1b, and α1d) adrenergic receptor binding affinity, functional activity of vascular and lower urinary tract tissues, and in vitro and in vivo selectivity was evaluated.

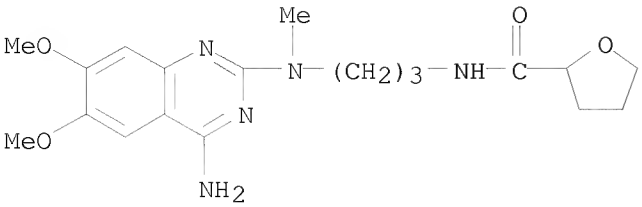
IT 81403-80-7, Alfuzosin

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(relevance of theor. mol. descriptors in QSAR anal. of α1-adrenergic receptor antagonists)
RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 62 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:710740 CAPLUS
DOCUMENT NUMBER: 131:306622
TITLE: Alpha-1-adrenoceptor blockade in the treatment of benign prostatic hyperplasia
AUTHOR(S): Lowe, F.
CORPORATE SOURCE: Department of Urology, St. Luke's-Roosevelt Hospital Center, New York, NY, 10019, USA
SOURCE: Prostate Cancer and Prostatic Diseases (1999), 2(3), 110-119
CODEN: PCPDFW; ISSN: 1365-7852
PUBLISHER: Stockton Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 85 refs. In light of the growing interest in the concept of "uroselectivity" and in the increased worldwide use of alpha-blockers for benign prostatic hyperplasia (BPH), this review evaluates the relative benefits of various alpha-blocking agents in the treatment of BPH. The pharmacol. and physiol. selectivity as well as the clin. efficacy and safety of alfuzosin, doxazosin (Cardura), tamsulosin (Flomax), and terazosin (Hytrin) are compared. In reviewing efficacy and safety, emphasis is given to 17 placebo-controlled, double-blind trials of these alpha-blockers published in peer-reviewed journals. This review also considers long-term data, effects on blood pressure, costs, and dose ranges.
IT 81403-80-7, Alfuzosin
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alpha-1-adrenoceptor blockade in treatment of benign prostatic hyperplasia)
RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



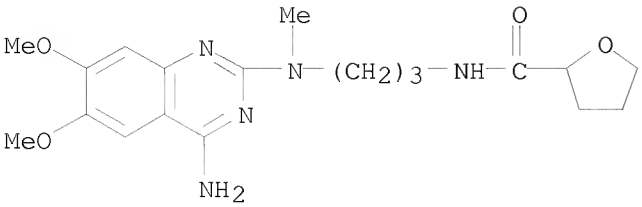
REFERENCE COUNT: 85 THERE ARE 85 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 63 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:709584 CAPLUS
DOCUMENT NUMBER: 132:30785
TITLE: Inverse agonism and neutral antagonism at α1a- and α1b-adrenergic receptor subtypes
AUTHOR(S): Rossier, Olivier; Abuin, Liliane; Fanelli, Francesca; Leonardi, Amedeo; Cotecchia, Susanna
CORPORATE SOURCE: Institute of Pharmacology and Toxicology, Universite de Lausanne, Lausanne, Switz.
SOURCE: Molecular Pharmacology (1999), 56(5), 858-866
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We have characterized the pharmacol. antagonism, i.e., neutral antagonism or inverse agonism, displayed by a number of α-blockers at two α1-adrenergic receptor (AR) subtypes, α1a- and α1b-AR. Constitutively activating mutations were introduced into the α1a-AR at the position homologous to A293 of the α1b-AR where activating mutations were previously described. Twenty-four α-blockers differing in their chemical structures were initially tested for their effect on the agonist-independent inositol phosphate response mediated by the constitutively active A271E and A293E mutants expressed in COS-7 cells. A selected number of drugs also were tested for their effect on the small, but measurable spontaneous activity of the wild-type α1a- and α1b-AR expressed in COS-7 cells. The results of our study demonstrate that a large number of structurally different α-blockers display profound neg. efficacy at both the α1a- and α1b-AR subtypes. For other drugs, the neg. efficacy varied at the different constitutively active mutants. The most striking difference concerns a group of N-arylpiperazines, including 8-[2-[4-(5-chloro-2-methoxyphenyl)-1-piperazinyl]ethyl]-8-azaspiro[4,5] decane-7,9-dione (REC 15/3039), REC 15/2739, and REC 15/3011, which are inverse agonists with profound neg. efficacy at the wild-type α1b-AR, but not at the α1a-AR.

IT 81403-80-7, Alfuzosin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(inverse agonism and neutral antagonism at α1a- and α1b-adrenergic receptor subtypes)

RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 64 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:688927 CAPLUS
DOCUMENT NUMBER: 131:281281
TITLE: Sustained-release alfuzosin and trial without catheter after acute urinary retention: a prospective, placebo-controlled trial
AUTHOR(S): Mcneill, S. A.; Daruwala, P. D.; Mitchell, I. D. C.; Shearer, M. G.; Hargreave, T. B.
CORPORATE SOURCE: Western General Hospital, Edinburgh, UK
SOURCE: BJU International (1999), 84(6), 622-627
CODEN: BJINFO; ISSN: 1464-4096
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

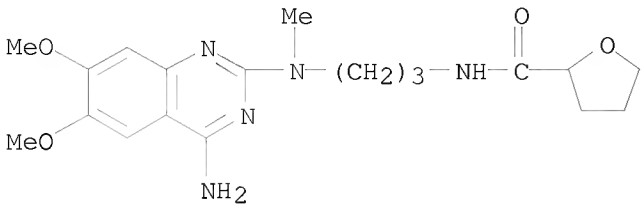
AB Objective: To establish whether the administration of sustained-release (SR) alfuzosin improves the outcome of a trial without catheter (TWOC) after an episode of acute urinary retention. Patients and methods: In a prospective, randomized, placebo-controlled trial, 81 patients with acute urinary retention related to benign prostatic obstruction received either SR alfuzosin (n=40), an α1-selective blocker, given at a dose of 5 mg twice daily, or placebo (n=41) for 48 h. The catheter was removed after 24 h of treatment. The main outcome measurement was success or failure of the TWOC. At the end of this double-blind phase the patients were followed up on an open basis. Results: After removal of the catheter, 42% of patients voided successfully, 22 of 40 (55%) with SR alfuzosin and 12 of 41 (29%) with placebo (P=0.03). The mean age of patients voiding successfully, regardless of treatment group, was 68.4 yr, while the mean age of those who were not successful was 72.9 yr (P=0.015). In an intention-to-treat anal. of outcome adjusted for this age difference, the benefit in favor of those receiving SR alfuzosin was not significant, but at P=0.052 there was a strong suggestion of a pos. treatment effect. The observed benefit remained significant in a per-protocol anal. adjusted for age. Taken together, these results indicate that treatment with SR alfuzosin was effective and that the observed benefit was not simply the effect of age difference between the groups. Of the 34 patients who voided successfully 23 (68%) required no further intervention within a mean follow-up of 7 mo. Conclusions: Treatment with SR alfuzosin is effective in improving the success rate of a TWOC after an episode of acute urinary retention, although older patients are less likely to void successfully. By reducing the nos. of men sent home with urinary catheters, such treatment may result in a reduction in the associated perioperative morbidity in those undergoing prostatic surgery, and is clearly desirable for the patients' comfort and convenience.

IT 81403-80-7, Alfuzosin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(sustained-release alfuzosin and trial without catheter after acute urinary retention in humans)

RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 65 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1999:647738 CAPLUS

DOCUMENT NUMBER: 131:252532

TITLE: Tamsulosin 0.4 mg once daily: effect on sexual function in patients with lower urinary tract symptoms suggestive of benign prostatic obstruction

AUTHOR(S): Hofner, K.; Claes, H.; De Reijke, T. M.; Folkestad, B.; Speakman, M. J.

CORPORATE SOURCE: Medizinische Hochschule, Hannover, Germany

SOURCE: European Urology (1999), 36(4), 335-341
CODEN: EUURAV; ISSN: 0302-2838

PUBLISHER: S. Karger AG

DOCUMENT TYPE: Journal

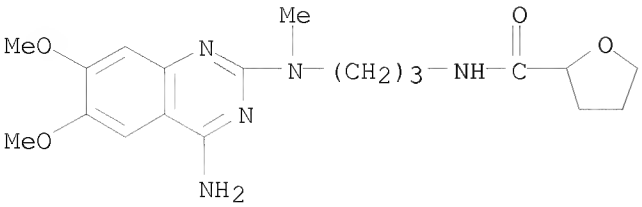
LANGUAGE: English

AB The effect of tamsulosin, 0.4 mg once daily, on sexual function was evaluated in comparison with that of placebo and alfuzosin, 2.5 mg 3 times daily, in patients with lower urinary tract symptoms suggestive of benign prostatic obstruction. Data from 830 patients randomized into three European multicenter studies with similar protocols were analyzed. The results indicated that tamsulosin, at the above dosage, is well tolerated and has no overall neg. impact on sexual function compared with placebo or alfuzosin. Compared with placebo, tamsulosin may even improve sexual function.

IT 81403-80-7, Alfuzosin
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sexual function in humans with lower urinary tract symptoms suggestive of benign prostatic obstruction response to tamsulosin vs. alfuzosin)

RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



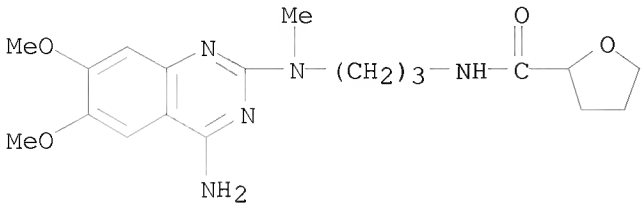
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 66 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:494791 CAPLUS
DOCUMENT NUMBER: 131:138711
TITLE: Clinical experience in Europe with uroselective α1-antagonists
AUTHOR(S): Debruyne, Frans M. J.; Van der Poel, Henk G.
CORPORATE SOURCE: Department of Urology, University Hospital Nijmegen, Nijmegen, NL-6500 HB, Neth.
SOURCE: European Urology (1999), 36(Suppl. 1), 54-58
CODEN: EUURAV; ISSN: 0302-2838
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 36 refs. α1-Adrenoreceptors are thought to be involved in prostate smooth muscle contractions and could hence play a role in the dynamic component of intravesical obstruction associated with symptomatic benign prostatic hyperplasia (BPH). Consequently, since the mid-eighties α-receptor blocking agents have been used for the treatment of BPH. Nonselective α-blockers are usually associated with systemic side-effects which result in exclusion or withdrawal of many patients from this form of treatment. With the availability of so-called uroselective α-blockers the management picture has changed, since it was anticipated that these compds. would cause lesser side-effects with at least the same, or even better, efficacy. Comparative clin. studies are essential for determining the eventual advantages of the uroselective α1-antagonists, and a large number of such studies have been performed worldwide studying the various available compds. European studies with terazosin showed clear superiority of the drug over placebo while causing only limited side-effects. Various other studies using α-blocking agents such as doxazosin, tamsulosin and alfuzosin yielded identical results. Especially with tamsulosin and alfuzosin, the side-effects were comparable with those encountered in the placebo group. About 7% of the patients using tamsulosin experienced retrograde ejaculation in one study, an effect which did not occur in the alfuzosin studies. Studies in Europe have also investigated the value of a combination of an α-blocker with a 5α-reductase inhibitor. Studies in which both alfuzosin and doxazosin were combined with the 5α-reductase inhibitor Proscar showed that the combination was not superior to α-blocker monotherapy; especially in the ALFIN study, alfuzosin monotherapy was superior to Proscar in the management of symptomatic BPH. European studies have also evaluated the effects of treatment with α1-receptor blockers on quality of life, sexuality, and socioeconomic factors.

IT 81403-80-7, Alfuzosin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(benign prostatic hyperplasia of humans treatment by

α1-adrenergic antagonists)
RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



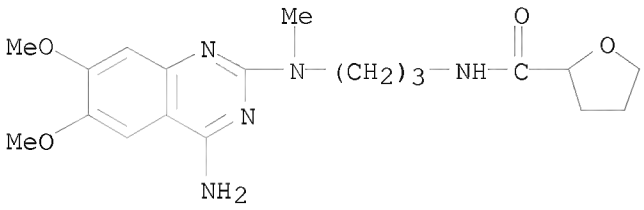
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 67 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:458556 CAPLUS
DOCUMENT NUMBER: 131:125391
TITLE: A meta-analysis of the efficacy and tolerability of α1-adrenoceptor antagonists in patients with lower urinary tract symptoms suggestive of benign prostatic obstruction
AUTHOR(S): Djavan, Bob; Marberger, Michael
CORPORATE SOURCE: Department of Urology, University of Vienna, Vienna, Austria
SOURCE: European Urology (1999), 36(1), 1-13
CODEN: EUURAV; ISSN: 0302-2838
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Literature reports were analyzed to determine whether the α1-adrenoceptor antagonists currently available for the treatment of lower urinary tract symptoms (LUTS) suggestive of benign prostatic obstruction (alfuzosin, terazosin, doxazosin and tamsulosin) can be distinguished with regard to clin. efficacy and/or tolerability. Indirect comparison of data derived from placebo-controlled studies involving 6333 patients and data derived from direct comparative studies involving 507 patients demonstrated that all of the above α1-adrenoceptor antagonists produced comparable improvements in LUTS and urinary flow. Total symptom score was in general improved by 30-40% and Qmax (mean end of study value relative to mean basal value) by 16-25%. The differences among these α1-adrenoceptor antagonists were related to their side effect profile. Alfuzosin (especially the sustained-release formulation) and tamsulosin (modified-release formulation, 0.4 mg) seem to be better tolerated than terazosin and doxazosin. The percentage of patients that withdrew due to bothersome side effects with alfuzosin and 0.4 mg tamsulosin was comparable to that with placebo (about 4-10%), whereas in the terazosin and doxazosin studies an addnl. 4-10% of the patients dropped out because they did not tolerate the therapy. Tamsulosin had less effect on blood pressure than alfuzosin (especially in elderly patients) and caused less symptomatic orthostatic hypotension than terazosin during orthostatic stress testing. It is concluded that all four of these α1-adrenoceptor antagonists seem to have similar efficacy in improving symptoms and flow. The differences among them are related to their side effect profile. Alfuzosin and tamsulosin appear to be better tolerated than doxazosin and terazosin.
IT 81403-80-7, Alfuzosin
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or

effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(efficacy and tolerability of α1-adrenoceptor antagonists in humans with lower urinary tract symptoms suggestive of benign prostatic obstruction)

RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 68 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1999:394166 CAPLUS

DOCUMENT NUMBER: 131:193730

TITLE: Effects of α1-adrenoceptor antagonists on agonist and tilt-induced changes in blood pressure: relationships to uroselectivity

AUTHOR(S): Hieble, J. Paul; Kolpak, David C.; McCafferty, Gerald P.; Ruffolo, Robert R., Jr.; Testa, Rodolfo; Leonardi, Amedeo

CORPORATE SOURCE: UW2510, Division of Pharmacological Sciences, SmithKline Beecham Pharmaceuticals, King of Prussia, PA, 19406, USA

SOURCE: European Journal of Pharmacology (1999), 373(1), 51-62
CODEN: EJPHAZ; ISSN: 0014-2999

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

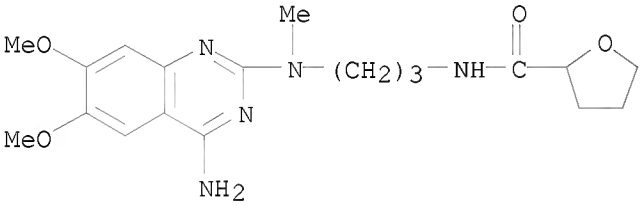
AB We evaluated the uroselectivity of a series of α1-adrenoceptor antagonists by comparing their potency against phenylephrine-induced increases in urethral perfusion pressure and diastolic blood pressure in the anesthetized rabbit and pithed rat. In the rabbit, Rec 15/2739 (N-[3-[4-(2-methoxyphenyl)-1-piperazinyl]propyl]-3-methyl-4-oxo-2-phenyl-4H-1-benzopyran-8-carboxamide) as well as analogs with a chlorine substituent on the methoxyphenyl ring (Rec 15/2869) or this substituent combined with the replacement of the Ph substituent on the pyran ring by cyclohexyl (Rec 15/3011) were 2-6-fold more potent against the urethral vs. vascular response to phenylephrine. Rec 15/2841 (N-[3-[4-(2-methoxyphenyl)-1-piperazinyl]propyl]-3-methyl-4-oxo-2-cyclohexyl-4H-1-benzopyran-8-carboxamide) was only 1.5-fold more potent against the urethral response. SL 89.0591 and tamsulosin also showed selectivity for the urethral response (2-2.5-fold), while the quinazolines produced equipotent blockade of urethral and vascular responses (selectivity ratio=0.9-1.1). The urethral selectivities of Rec 15/2739 and its derivs. were confirmed by evaluation of the response to tilt in sedated, hypovolemic rabbits. Phenylephrine challenge assays did not show any of the antagonists, with the exception of terazosin at 300 μg kg-1, to be uroselective in the rat (selectivity ratios=0.2-1.5); potentiation of tilt-induced hypotension in the anesthetized rat showed substantial

differences from the rabbit, with Rec 15/2739, but not Rec 15/3011 and Rec 15/2841 showing orthostatic effects equivalent to that observed for prazosin. Hence, Rec 15/2739 was uroselective in the rabbit, but not in the rat, while two of its close structural analogs were highly uroselective in both species. An assay for orthostatic activity in the conscious rat yielded different results, showing prazosin and terazosin, but not Rec 15/2739, to cause a reversal of the pressor response to tilt. Hence, the apparent uroselectivity of an α1-adrenoceptor antagonist is both species- and assay-dependent.

IT 81403-80-7, Alfuzosin
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of α1-adrenoceptor antagonists on agonist and tilt-induced changes in blood pressure and structure-activity relationships to uroselectivity)

RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 69 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1999:327260 CAPLUS

DOCUMENT NUMBER: 131:97273

TITLE: Selective effects of alfuzosin and doxazosin with intraduodenal administration on urethral pressure of cats

AUTHOR(S): Yang, Zhi-Yui; Ren, Lei-Ming; Wu, Zhan-Jun; Fu, Shao-Xuan; Li, Yun-Shan

CORPORATE SOURCE: Department of Pharmacology, Hebei Medical University, Shijiazhuang, 050017, Peop. Rep. China

SOURCE: Zhongguo Yaoli Xuebao (1999), 20(5), 431-434
CODEN: CYLPDN; ISSN: 0253-9756

PUBLISHER: Kexue Chubanshe

DOCUMENT TYPE: Journal

LANGUAGE: English

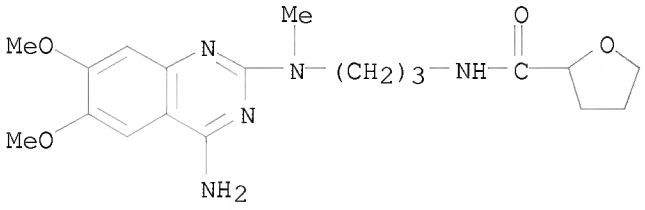
AB To observe the selective effects of alfuzosin (Alf) and doxazosin (Dox) on the urethral pressure by different administration routes, the urethral pressure of the anesthetized cat was increased by elec. stimulation of the hypogastric nerve. The different effects of Alf or Dox on the arterial blood pressure and urethral pressure between intraduodenal administration (id) and i.v. infusion (iv) were compared. When the hypogastric nerve was stimulated by elec. stimulation (10 Hz, 25 V), the ratios of ED20(BP)/ED50(UP) id to ED20(BP)/ED50(UP) iv were 10.9:4.3 for Alf, and 3.1:2.1 for Dox. The reduction in urethral pressure induced by id Alf was greater than that by iv Alf. Dox did not show any difference in its effects by 2 administration routes. Intraduodenal administration of Alf, but not Dox, selectively decreased the urethral pressure elevated by elec.

stimulation. The uroselectivity of id Alf was not due to the species difference in its bioavailability and biotransformation.

IT 81403-80-7, Alfuzosin
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(selective effects of alfuzosin and doxazosin with intraduodenal administration on urethral pressure of cats)

RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 70 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1998:666544 CAPLUS

DOCUMENT NUMBER: 130:60703

TITLE: Three-year prospective study of 3228 clinical BPH patients treated with alfuzosin in general practice

AUTHOR(S): Lukacs, B.; Grange, J. C.; Comet, D.; McCarthy, C.

CORPORATE SOURCE: BPH Group in General Practice, Urology Department, Hospital Tenon, Paris, Fr.

SOURCE: Prostate Cancer and Prostatic Diseases (1998), 1(5), 276-283
CODEN: PCPDFW; ISSN: 1365-7852

PUBLISHER: Stockton Press

DOCUMENT TYPE: Journal

LANGUAGE: English

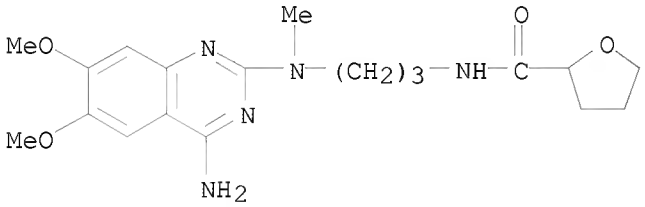
AB Our objectives were to investigate (a) the magnitude and durability of symptom score reduction and HRQL score improvement (including sexual drive); (b) adverse outcomes; and (c) progression to acute urinary retention and prostate surgery up to three years of treatment with alfuzosin. Three thousand two hundred and twenty-eight BPH-patients out of 812 centers were included in a prospective three-year open-labeled study and treated with alfuzosin (immediate release formulation) at the recommended dosage. A symptom score (Boyarsky modified) and a 20-item BPH specific HRQL score including three questions of sexuality (UrolifeTM BPH QoL 20) were self-administered at baseline, 3, 6, 12, 18, 24, 30, and 36 mo. Two thousand five hundred and seventy-nine patients (79.9%) completed the study at the end of three years. Symptom score was significantly reduced by 54% at 3 mo and this reduction was maintained up to 36 mo (-48.4%); HRQL score was significantly improved by 45.4% at 12 mo and this improvement was maintained up to 36 mo (+43.4%). Alfuzosin was well tolerated: the quant. and qual. distribution of adverse events was similar to that previously observed in placebo-controlled studies (vertigo/dizziness: 2.1%). Adverse events accounted for 4.2% of the drop-outs. 120 patients (3.7%) were operated on for BPH and nine patients (0.3%) experienced acute urinary retention. This medical outcomes study confirms the long-term safety profile of alfuzosin in the naturalistic conditions of general

practice and highlights the need to measure HRQL in the context of patient's preferences.

IT 81403-80-7, Alfuzosin
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(three-year prospective study of 3228 clin. humans with benign prostatic hyperplasia treated with alfuzosin)

RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 71 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1998:637676 CAPLUS

DOCUMENT NUMBER: 130:32752

TITLE: Sustained-release alfuzosin, finasteride and the combination of both in the treatment of benign prostatic hyperplasia

AUTHOR(S): Debruyne, F. M. J.; Jardin, A.; Colloi, D.; Resel, L.; Witjes, W. P. J.; Delauche-Cavallier, M. C.; McCarthy, C.; Geffriaud-Ricouard, C.

CORPORATE SOURCE: Department of Urology, University Hospital Nijmegen, Nijmegen, NL-6500 HB, Neth.

SOURCE: European Urology (1998), 34(3), 169-175
CODEN: EUURAV; ISSN: 0302-2838

PUBLISHER: S. Karger AG

DOCUMENT TYPE: Journal

LANGUAGE: English

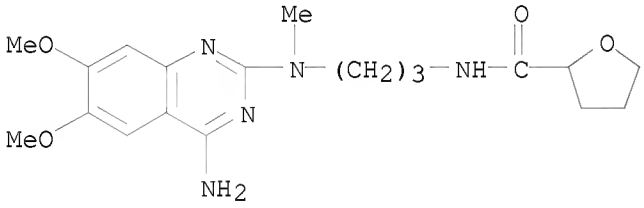
AB This study assess the additive benefit of combining an α1-blocker and a 5α-reductase inhibitor. This European, randomized, double-blind, multicenter trial involved 1.051 patients with lower urinary tract symptoms related to benign prostatic hyperplasia. Patients received sustained release (SR) alfuzosin (n = 358), a selective α1-blocker given at a dose of 5 mg twice daily without dose titration; finasteride (n = 344), 5 mg once daily, or both drugs (n = 349), for 6 mo. Primary efficacy criteria were symptomatic improvement (International Prostate Symptom Score: I-PSS) and maximum flow rate (Qmax). Safety was assessed by monitoring adverse events. Symptomatic improvement was significantly higher from the 1st month of treatment with SR alfuzosin, alone or in combination; mean changes in I-PSS vs. baseline at end-point were -6.3 and -6.1, resp., compared with -5.2 with finasteride alone (SR alfuzosin vs. finasteride, p = 0.01; combination vs. finasteride, p = 0.03). The percentages of patients with a decrease in I-PSS of at least 50% were 43, 42 and 33% for SR alfuzosin, the combination and finasteride, resp. (SR alfuzosin vs. finasteride, p = 0.008; combination vs. finasteride, p = 0.009). In the overall population, increases in Qmax were greater with SR alfuzosin and the combination, compared with finasteride alone after 1 mo

of therapy, but changes at end-point were similar in the three treatment groups. In those 47% of patients likely to be obstructed (baseline Qmax < 10 mL/s), however, mean increases in Qmax were significantly higher with SR alfuzosin, alone or in combination, whatever the visit. Finasteride, alone or in combination, significantly impaired sexual function. The incidence of postural symptoms was low and similar in the three treatment groups. In this 6-mo trial, SR alfuzosin was more effective than finasteride, with no addnl. benefit in combining both drugs.

IT 81403-80-7, Alfuzosin
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sustained-release alfuzosin, finasteride and combination in treatment of benign prostatic hyperplasia in humans)

RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 72 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1998:544512 CAPLUS

DOCUMENT NUMBER: 129:297769

ORIGINAL REFERENCE NO.: 129:60577a,60580a

TITLE: Clinical uroselectivity of alfuzosin in the treatment of benign prostatic hyperplasia

AUTHOR(S): Kirby, Roger S.

CORPORATE SOURCE: Department of Urology, St. George's Hospital, London, UK

SOURCE: European Urology (1998), 33(Suppl. 2, Uroselectivity: Myth or Reality?), 19-27
CODEN: EUURAV; ISSN: 0302-2838

PUBLISHER: S. Karger AG

DOCUMENT TYPE: Journal; General Review

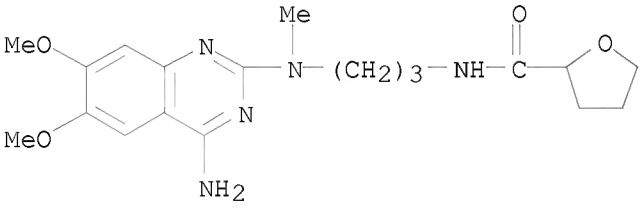
LANGUAGE: English

AB A review with 43 refs. The efficacy of alfuzosin in improving lower urinary tract symptoms and relieving bladder outlet obstruction has been demonstrated in numerous short- and long-term placebo-controlled studies and large-scale open studies, involving over 16,000 patients with symptomatic benign prostatic hyperplasia (BPH). Treatment with sustained release alfuzosin (5 mg twice daily) for 3 mo resulted in a 5-point reduction in the International Prostate Symptom Score and a 29% increase in urinary flow rate. The benefits of alfuzosin have been confirmed in general practice. A 1-yr prospective study of 5,849 men with clin. BPH treated with alfuzosin showed a 51% reduction in mean total symptom score, with a 56% decrease in mean irritative symptoms. Improvement in health-related quality of life of 3 yr' duration have been recorded, including a reduction in the frequency of both diurnal and nocturnal micturition. Alfuzosin has a good safety profile. Unlike most other α1-blockers, a low risk of

first-dose effect is seen, conveniently eliminating the necessity of dose titration at initiation of therapy. Postural symptoms related to orthostatic hypotension (a common side-effect of α1-blockers) are infrequent, including in the elderly and hypertensives. Central nervous system effects are also limited due to poor penetration of the blood-brain barrier. In conclusion, the pos. benefits/risk ratio of alfuzosin allows it to be classified as a uroselective α1-blocker, which provides a beneficial contribution to the management of symptomatic BPH.

IT 81403-80-7, Alfuzosin
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alfuzosin clin. uroselectivity humans with benign prostatic hyperplasia)

RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 73 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1998:542007 CAPLUS
DOCUMENT NUMBER: 129:298258
ORIGINAL REFERENCE NO.: 129:60697a,60700a
TITLE: Efficacy and safety of sustained-release alfuzosin 5 mg in patients with benign prostatic hyperplasia
AUTHOR(S): Buzelin, J. M.; Roth, S.; Geffriaud-Ricouard, C.; Delauche-Cavallier, M. C.
CORPORATE SOURCE: The ALGEBI Study Group, Department of Urology, CHU Hotel-Dieu, Nantes, F-44035, Fr.
SOURCE: European Urology (1997), 31(2), 190-198
CODEN: EUURAV; ISSN: 0302-2838
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English

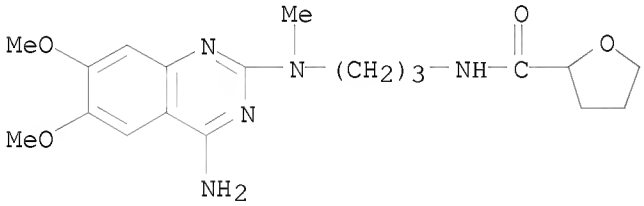
AB The purpose of this study was to assess the efficacy and safety of a sustained-release (SR) formulation of alfuzosin, a selective α1-blocker, in patients with symptomatic benign prostatic hyperplasia (BPH). A total of 390 men were randomly assigned to receive SR-alfuzosin (n = 194), 5 mg twice daily without dose titration, or placebo (n = 196) for 12 wk. Of the patients included, 47% had concomitant cardiovascular disease, mainly hypertension or coronary heart disease. SR-alfuzosin significantly improved urinary symptoms vs. placebo assessed using the I-PSS (-31 vs. -18%,p = 0.007) and Boyarsky (-30 vs. -16%, p < 0.001) scores, with a direct correlation between both scores. Maximum flow rate increased significantly with SR-alfuzosin (+2.4 mL/s, i.e. +29%) compared with placebo (+1.1 mL/s, i.e. +14%, p = 0.006). Residual urine was also significantly reduced with SR-alfuzosin. Overall, SR-alfuzosin was as well tolerated as placebo. Nine patients dropped out for adverse

events with SR-alfuzosin (4.6%) and 14(7.1%) with placebo. The incidence of vasodilation-related events (dizziness, postural symptoms, headache) with SR-alfuzosin (3.1%) was similar to that of placebo (3.6%). No first-dose effect was observed compared with placebo. The reduction in supine blood pressure with SR-alfuzosin was minor (≤5 mm Hg), both in normotensive and hypertensive patients. SR-alfuzosin is an effective treatment of symptoms related to BPH that shows a good safety profile in normotensive and hypertensive patients, without the need of dose titration

IT 81403-80-7, Alfuzosin
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alfuzosin sustained-release efficacy and safety in men with benign prostatic hyperplasia)

RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 74 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1998:521381 CAPLUS

DOCUMENT NUMBER: 129:285774

ORIGINAL REFERENCE NO.: 129:58093a,58096a

TITLE: Effects of short-term treatment with the α1-blocker alfuzosin on urodynamic pressure/flow parameters in patients with benign prostatic hyperplasia

AUTHOR(S): Martorana, Giuseppe; Giberti, Claudio; Di Silverio, Franco; von Heland, Magnus; Rigatti, Patrizio; Colombo, Renzo; Casadei, Gianluigi; Pacifico, Paolo

CORPORATE SOURCE: Urology Department, University of Bologna, Italy

SOURCE: European Urology (1997), 32(1), 47-53
CODEN: EUURAV; ISSN: 0302-2838

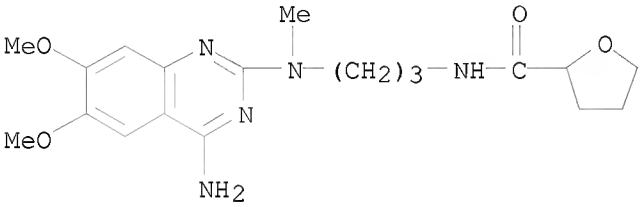
PUBLISHER: S. Karger AG

DOCUMENT TYPE: Journal

LANGUAGE: English

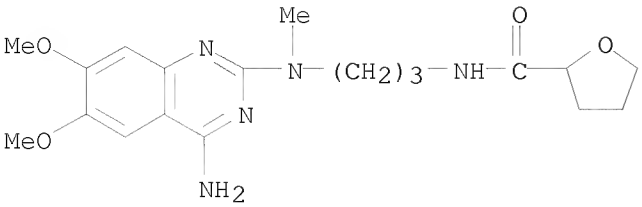
AB The objective of this double-blind, placebo-controlled urodynamic pressure/flow study was to assess the efficacy of short-term treatment with the α1-blocker alfuzosin in outflow obstruction of patients with symptomatic benign prostatic hyperplasia (BPH). Urodynamic pressure/flow parameters were assessed after 2 wk of placebo run-in, 4 wk of placebo (47 patients) or 2.5 mg t.i.d. alfuzosin treatment (47 patients), followed by an 8-wk extension period with alfuzosin (single-blind). Four weeks of alfuzosin treatment significantly increased maximum flow (+29.0%) and decreased detrusor pressure at maximum flow (-30.2%), detrusor opening pressure (-39.4%) and maximum detrusor pressure (-28.7%). Short-term alfuzosin treatment improved outflow conditions in BPH by reducing prostatic urethral obstruction.

IT 81403-80-7, Alfuzosin
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α1-blocker alfuzosin short-term treatment effects on urodynamics in humans with benign prostatic hyperplasia)
RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 75 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1998:461677 CAPLUS
DOCUMENT NUMBER: 129:232257
ORIGINAL REFERENCE NO.: 129:47231a
TITLE: Development and improvement of manufacturing processes from dimethyl (N-cyanimido-dithiocarbonate) on the basis of theoretical considerations
AUTHOR(S): Reiter, Jozsef; Pongo, Laszlo
CORPORATE SOURCE: EGIS Gyogyszergyar Rt., Budapest, Hung.
SOURCE: Magyar Kemikusok Lapja (1998), 53(7), 326-334
CODEN: MGKLAL; ISSN: 0025-0163
PUBLISHER: Magyar Kemikusok Egyesulet
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Hungarian
AB Based on a detailed theor. study of the reactions of di-Me N-cyanoimidodithiocarbonate with amines and hydrazine new, independent synthetic routes to chlorohexidine (I), lamtidine and alfuzosin were reviewed with 29 refs. meeting the most recent requirements. By slight modification of the synthetic route to I based on the results of the above theor. studies a considerable increase of the yield was achieved. In search towards new type diuretics a new reaction was observed characterized with a new leaving group.
IT 81403-80-7P, Alfuzosin
RL: IMF (Industrial manufacture); PREP (Preparation)
(development and improvement of manufacturing processes from di-Me N-cyanimido-dithiocarbonate on the basis of theor. considerations)
RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)

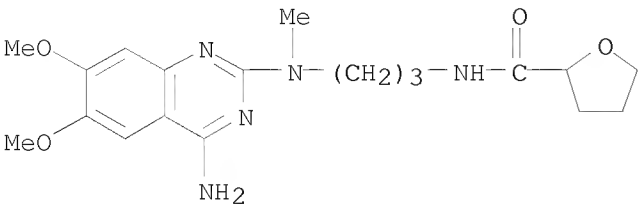


L5 ANSWER 76 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1998:409349 CAPLUS
DOCUMENT NUMBER: 129:131166
ORIGINAL REFERENCE NO.: 129:26673a,26676a
TITLE: Relationship between the effects of alfuzosin on rat urethral and blood pressures and its tissue concentrations
AUTHOR(S): Martin, D. J.; Lluel, P.; Pouyet, T.; Rauch-Desanti, C.; Angel, I.
CORPORATE SOURCE: Synthelabo Recherche, Internal Medicine Research, Rueil-Malmaison, 92504, Fr.
SOURCE: Life Sciences (1998), 63(3), 169-176
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB This study was undertaken to establish the α1-antagonist effects of alfuzosin on phenylephrine-induced increases in urethral and arterial blood pressures at 1 and 6 h post dosing (10 mg/kg, p.o.). At each time, plasma and prostatic concns. of alfuzosin were measured and correlations between tissue concns. and pharmacol. effects were calculated At one and six hours post dosing, alfuzosin markedly shifted the urethral and arterial dose response curve to phenylephrine. At one hour, prostatic concentration was 4.1 times greater than plasma concentration (363 ng/g vs. 88 ng/mL) and at 6 h this ratio reached 8.6 times (167 ng/g vs. 20 ng/mL). By taking together the data points obtained at 1 an 6 h the authors showed that the effects of alfuzosin on urethral pressure were correlated with prostate levels (r= 0.906) and the effects on arterial blood pressure were correlated with plasma levels (r= 0.941). These results suggest that a preferential distribution of alfuzosin in prostatic tissue may play a role in its functional uroselectivity.

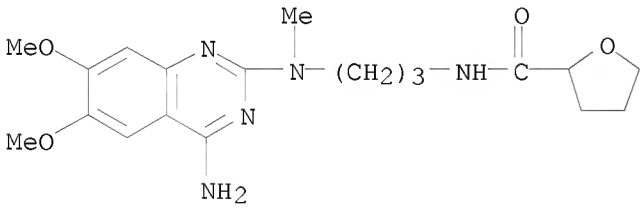
IT 81403-80-7, Alfuzosin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(relationship between the effects of alfuzosin on rat urethral and blood pressures and its tissue concns.)

RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 77 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1998:323529 CAPLUS
DOCUMENT NUMBER: 129:67
ORIGINAL REFERENCE NO.: 129:11a,14a
TITLE: α1-blockers for the treatment of benign prostatic hypertrophy (BPH)
AUTHOR(S): Thesen, Rolf
CORPORATE SOURCE: Arzneimittelinformationsstelle, ABDA, Eschborn, D-65760, Germany
SOURCE: Pharmazeutische Zeitung (1998), 143(21), 1746-1754
CODEN: PHZIAP; ISSN: 0031-7136
PUBLISHER: Govi-Verlag Pharmazeutischer Verlag
DOCUMENT TYPE: Journal; General Review
LANGUAGE: German
AB A review with 27 refs. is given on the α1-blockers terazosin, doxazosin, alfuzosin, and tamsulozin for the treatment of benign prostatic hyperplasia including dosage, effects and side effects, mechanism of action, pharmacokinetics, and clin. trials.
IT 81403-80-7, Alfuzosin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α1-blockers for the treatment of benign prostatic hypertrophy)
RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)

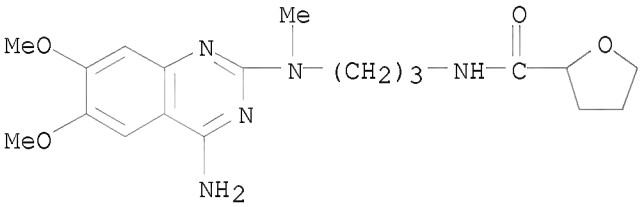


L5 ANSWER 78 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1998:304032 CAPLUS
DOCUMENT NUMBER: 129:62431
ORIGINAL REFERENCE NO.: 129:12765a,12768a
TITLE: Computer modeling of size and shape descriptors of α1-adrenergic receptor antagonists and quantitative structure-affinity/selectivity relationships
AUTHOR(S): Montorsi, Monia; Menziani, M. Cristina; Cocchi, Marina; Fanelli, Francesca; De Benedetti, Pier G.
CORPORATE SOURCE: Dipartimento di Chimica, Universita di Modena, Modena, 41100, Italy
SOURCE: Methods (Orlando, Florida) (1998), 14(3), 239-254
CODEN: MTHDE9; ISSN: 1046-2023
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Computational chemical and mol. modeling procedures allow the authors to

define and compute ad hoc size and shape descriptors on the different prototropic forms assumed by drugs in biotest solns. Together with exptl. data measured on a well-identified target receptor, these descriptors are essential elements for obtaining simple, consistent, comparable, and easily interpretable theor. quant. structure-activity relation (QSAR) models based on the ligand similarity-target receptor complementarity paradigm. In this context, quant. size and shape affinity/subtype selectivity relationships have been modeled for a large set of very heterogeneous α1a-, α1b-, and α1d- adrenergic receptor antagonists. The linear QSAR models generated have been validated by predicting both binding affinity and selectivity of a test set of noncongeneric antagonists. The satisfactory results obtained highlight both the simplicity and the versatility of the approach presented.

IT 81403-80-7, Alfuzosin
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(computer modeling of size and shape descriptors of α1-adrenergic receptor antagonists and quant. structure-affinity/selectivity relationships)

RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 79 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1998:55546 CAPLUS
DOCUMENT NUMBER: 128:119675
ORIGINAL REFERENCE NO.: 128:23363a,23366a
TITLE: Useful formulations of acid addition salt drugs
INVENTOR(S): Pero, Ronald W.
PATENT ASSIGNEE(S): Oxigene, Inc., USA
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9800159	A1	19980108	WO 1997-US10829	19970623

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,

GN, ML, MR, NE, SN, TD, TG

CA 2258965	A1	19980108	CA 1997-2258965	19970623
AU 9734075	A	19980121	AU 1997-34075	19970623
AU 738165	B2	20010913		
EP 954327	A1	19991110	EP 1997-930184	19970623
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2000516204	T	20001205	JP 1998-504223	19970623
ZA 9705755	A	19980223	ZA 1997-5755	19970627
PRIORITY APPLN. INFO.:			US 1996-673341 A	19960628
			WO 1997-US10829 W	19970623

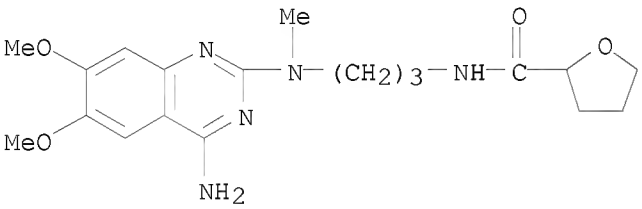
OTHER SOURCE(S): MARPAT 128:119675

AB Disclosed are methods and formulations for administering acid addition salts of compds. of R1(CH2)nN+HR2R3·X- or R1(CH2)nN+R2R3R4·X-, wherein R1 comprises an aryl or alkyl group with a hydrogen bond acceptor site accessible to interaction with the tertiary nitrogen or the quaternary ammonium ion, R2, R3 and R4 are alkyl or aryl groups, and X is an anion. A sterile injectable formulation of a liquid vehicle containing the acid addition salt in solution is adjusted in pH for reducing the development of undesirable side effects of the compound or provided at a pH 5.5-7.0. An i.m. injection containing the salt at ≥50 mg/mL and at a pH 5.5-7.0, is safely administered. UV spectral anal. of metoclopramide (I) solns. adjusted in pH 4.8-6.0 showed a very sharp change in maximal absorption of I solns. around pH 5, indicating shifting of equilibrium between the 2 conformational forms of I, namely, one with the pH sensitive hydrogen bond present and one without it.

IT 81403-80-7D, Alfuzosin, acid addition salts
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pH-controlled i.m. injections for acid addition salts of drugs to avoid side effects)

RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 80 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1997:705693 CAPLUS

DOCUMENT NUMBER: 127:303315

ORIGINAL REFERENCE NO.: 127:59151a,59154a

TITLE: Comparison of tamsulosin with alfuzosin in the treatment of patients with lower urinary tract symptoms suggestive of bladder outlet obstruction (symptomatic benign prostatic hyperplasia)

AUTHOR(S): Buzelin, J. M.; Fonteyne, E.; Kontturi, M.; Witjes, W. P. J.; Khan, A.

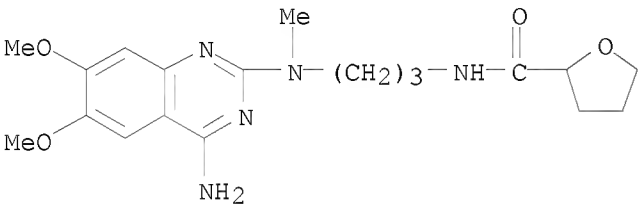
CORPORATE SOURCE: Hotel Dieu, Nantes, Fr.

SOURCE: British Journal of Urology (1997), 80(4), 597-605

CODEN: BJURAN; ISSN: 0007-1331
PUBLISHER: Blackwell
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The efficacy and tolerability of the α1A-subtype-selective adrenergic antagonist tamsulosin were compared with those of the non-subtype-selective agent alfuzosin in the treatment of patients with lower urinary tract symptoms suggestive of bladder outlet obstruction, often termed symptomatic benign prostatic hyperplasia (BPH). The study comprised patients with benign prostatic enlargement and lower urinary tract symptoms suggestive of bladder outlet obstruction (symptomatic BPH) who received 0.4 mg tamsulosin once daily or 2.5 mg alfuzosin 3 times daily for 12 wk. The response was assessed by measurements of maximum urinary flow rate (Qmax), a symptom score (Boyarsky) and blood pressure. Tamsulosin and alfuzosin produced comparable improvements in Qmax and total Boyarsky symptom score. Both treatments were well tolerated with respect to adverse events. Tamsulosin had no effect on basal blood pressure but alfuzosin reduced both standing and supine blood pressure. Tamsulosin is the 1st adrenoceptor antagonist that is selective for the α1A-subtype; this specificity may explain its lack of effect on blood pressure compared with alfuzosin, an agent that is not receptor subtype specific. This finding may partly explain why tamsulosin, in contrast to other currently available α1-adrenoceptor antagonists, can be administered without dose titration Another advantage compared with alfuzosin (and prazosin) is the once-daily dosage regimen of tamsulosin.

IT 81403-80-7, Alfuzosin
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(symptomatic benign prostatic hyperplasia of humans treatment by tamsulosin vs.)
RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 81 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1997:457537 CAPLUS
DOCUMENT NUMBER: 127:171463
ORIGINAL REFERENCE NO.: 127:33061a,33064a
TITLE: Comparative alpha-1 adrenoceptor subtype selectivity and functional uroselectivity of alpha-1 adrenoceptor antagonists
AUTHOR(S): Martin, D. J.; Lluel, P.; Guillot, E.; Coste, A.; Jammes, D.; Angel, I.
CORPORATE SOURCE: Dep. of Internal Medicine, Synthelabo Recherche, Rueil-Malmaison, 92504, Fr.
SOURCE: Journal of Pharmacology and Experimental Therapeutics

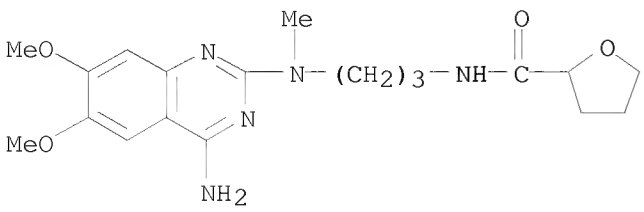
(1997), 282(1), 228-235
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We investigated the relevance of selectivity for a given alpha-1-adrenoceptor subtype for in vivo uroselectivity of several alpha-1-adrenoceptor antagonists (alfuzosin, doxazosin, prazosin, tamsulosin, terazosin and 5-Me-urapidil). Comparison of the affinities of these alpha-1-adrenoceptor antagonists at the cloned alpha-1a, alpha-1b and alpha-1d-adrenoceptor subtypes revealed that tamsulosin and 5-Me-urapidil showed selectivity for the alpha-1a subtype. No significantly correlations were found between the affinities for alpha-1b or alpha-1d-adrenoceptors and the pKB values obtained against phenylephrine-induced contraction of the rabbit prostate in vitro. In contrast, the antagonist potencies in rabbit prostate were correlated ($r = 0.89$, $P < .05$) with the pKi values for the alpha-1a-adrenoceptor subtype. However, the pKB values were consistently smaller (by 0.6 to 1.0 log unit) than the pKi values for the alpha-1a-adrenoceptor subtype, a result that suggests that the alpha-1-adrenoceptor mediating urethral contractions does not have all the characteristics of the alpha-1a-adrenoceptor. The simultaneous measurement of urethral and arterial pressures in the same conscious male rat allows evaluation of the functional uroselectivity of these antagonists based on their resp. effects on both pressures. Dose ranges were selected according to effects on urethral pressure and most antagonists were found effective within the 3 to 100 μg/kg i.v. range. Alfuzosin markedly decreased urethral pressure and either did not decrease blood pressure (10-30 μg/kg) or slightly decreased it at the highest dose tested (100 μg/kg). Doxazosin did not produce sustained redns. in urethral pressure until a dose of 30 μg/kg. Blood pressure was not reduced until 100 μg/kg. Prazosin reduced urethral pressure and blood pressure within the same dose-range whereas terazosin did not decrease urethral pressure at doses that significantly decreased blood pressure (30 and 100 μg/kg). 5-Me-urapidil, an alpha-1a-selective compound did not significantly modify urethral and blood pressure whereas tamsulosin, another alpha-1a-selective compound reduced urethral pressure and blood pressure within the same dose range. In conclusion, in the conscious male rate the functional uroselectivity is not correlated with a selective affinity for the alpha-1a-adrenoceptor subtype.

IT 81403-80-7, Alfuzosin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(uroselectivity and adrenoreceptor subtype specificity of alpha-1 adrenoceptor antagonists)

RN 81403-80-7 CAPLUS

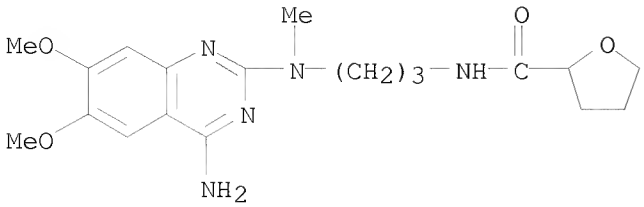
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



L5 ANSWER 82 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1997:446137 CAPLUS
DOCUMENT NUMBER: 127:117211
ORIGINAL REFERENCE NO.: 127:22465a,22468a
TITLE: Clinical uroselectivity: evidence from patients treated with slow-release alfuzosin for symptomatic benign prostatic obstruction
AUTHOR(S): Buzelin, J.M.; Delauche-Cavallier, M.C.; Roth, S.; Geffriaud-Ricouard, C.; Santoni, J.P.
CORPORATE SOURCE: Department of Urology, CHU Hotel Dieu, Nantes, Fr.
SOURCE: British Journal of Urology (1997), 79(6), 898-906
CODEN: BJURAN; ISSN: 0007-1331
PUBLISHER: Blackwell
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Our aim was to assess the safety profile of slow-release (SR) alfuzosin in the treatment of benign prostatic obstruction (BPO), with special attention to orthostatic blood pressure changes, postural symptoms and efficacy. Two placebo-controlled studies involving 588 patients (292 receiving SR alfuzosin 5 mg twice daily and 296 a placebo) were pooled; 51% of the patients were ≥65 yr of age and 43% had associated cardiovascular disease including hypertension and/or were receiving concomitant antihypertensive drugs. SR alfuzosin was very well tolerated with an overall incidence of adverse events similar to that of placebo (18.5% and 15.8% of patients, resp.) and an overall incidence of withdrawal from therapy for adverse events lower than that of placebo (3.4% and 5.7%, resp.). Adverse events potentially related to vasodilatation were infrequent with SR alfuzosin (the same incidence as with placebo, i.e. 2.7% of patients) and these adverse events occurred mainly during the first month of alfuzosin treatment. The effect on supine blood pressure was minimal. In the subgroups of elderly and hypertensive patients treated with SR alfuzosin, the cumulative incidence of asymptomatic orthostatic hypotension during the first month of treatment was slightly higher than with placebo with no objective consequences on the incidence of adverse events. The clin. efficacy of SR alfuzosin was confirmed by a significant improvement in urinary symptoms and a significant increase in maximum flow rates. SR alfuzosin (10 mg/day) can be administered safely without titration in patients with BPO, even in elderly and hypertensive patients. Its favorable benefit/risk ratio allows alfuzosin to be classified as a clin. uroselective α1-blocker. Specific anal. of orthostatic changes in blood pressure is important when assessing the safety profile of an α1-blocker in patients with BPO.

IT 81403-80-7, Alfuzosin
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(slow-release alfuzosin for symptomatic benign prostatic obstruction)
RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)

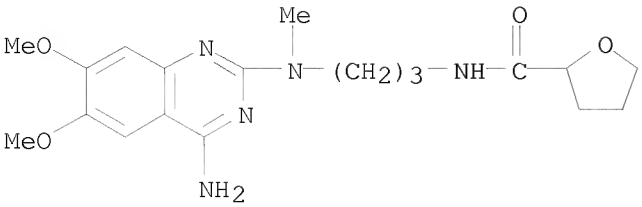


L5 ANSWER 83 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1997:331431 CAPLUS
DOCUMENT NUMBER: 127:60478
ORIGINAL REFERENCE NO.: 127:11393a,11396a
TITLE: Analysis of α1-adrenoceptors in rabbit lower urinary tract and mesenteric artery
AUTHOR(S): Van der Graaf, Pieter H.; Deplanne, Valerie; Duquenne, Chantal; Angel, Itzchak
CORPORATE SOURCE: Synthelabo Recherche (L.E.R.S.), Department of Internal Medicine, B.P. 248, 10 rue des Carrieres, Rueil Malmaison, 92500, Fr.
SOURCE: European Journal of Pharmacology (1997), 327(1), 25-32
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In this study, we have investigated the effects of a series of α1-adrenoceptor antagonists on the phenylephrine-mediated contractions of rabbit isolated prostate, urethra, trigone and mesenteric artery. With the exception of RS-17053 (N-[2-(2-cyclopropylmethoxyphenoxy)ethyl]-5-chloro-α,α-dimethyl-1H-indole-3-ethanamine hydrochloride), the antagonists displayed the lowest potency in the urethra. Catecholamine uptake1 and uptake2 appeared not to be the cause for the low pKB /pA2 values obtained in the urethra because cocaine and corticosterone had no effect on the potency of phenylephrine in this tissue. The low potencies displayed by prazosin, RS-17053 and HV723 (α-ethyl-3,4,5-trimethoxy-α-(3-((2-(2-methoxyphenoxy)ethyl)amino)propyl)benzene-acetonitrile fumarate) suggest that the functional receptors in all four tissues belong to the α1L-adrenoceptor class. Whether or not the significant between-tissue differences in antagonist potencies are due to heterogeneity of this receptor class remains to be elucidated.

IT 81403-80-7, Alfuzosin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(pharmacol. characteristics of the α1-adrenoceptors in rabbit lower urinary tract and mesenteric artery)

RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 84 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1997:127459 CAPLUS
DOCUMENT NUMBER: 126:126928
ORIGINAL REFERENCE NO.: 126:24382a
TITLE: Treatment and prevention of prostatic disease, including prostate cancer and benign prostatic hyperplasia, with compounds binding to sex hormone-binding globulin (SHBG), and method for therapeutic compound identification
INVENTOR(S): Smith, Roy G.; Rosner, William; Nakhla, Atif M.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA; St. Luke's Roosevelt Hospital Center; Smith, Roy G.; Rosner, William; Nakhla, Atif M.
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9640150	A1	19961219	WO 1996-US8873	19960605
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2222625	A1	19961219	CA 1996-2222625	19960605
AU 9659841	A	19961230	AU 1996-59841	19960605
EP 833641	A1	19980408	EP 1996-917173	19960605
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 11507050	T	19990622	JP 1996-501341	19960605

PRIORITY APPLN. INFO.: US 1995-484633 A 19950607
WO 1996-US8873 W 19960605

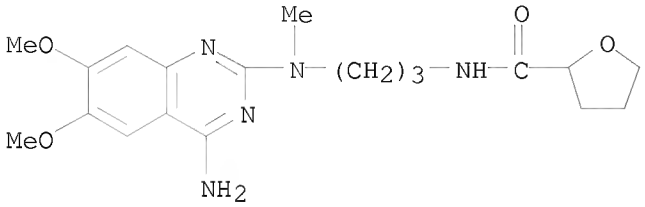
AB A method for treating and preventing benign prostatic hyperplasia (BPH) and prostatic carcinoma involves administering a therapeutically effective amount of a compound which binds to SHBG and antagonizes the SHBG-mediated effects of both estradiol and 5α-androstan-3α,17β-diol by preventing the binding of estradiol and 5α-androstan-3α,17β-diol. Also disclosed are the compds. which bind SHBG and prevent the binding of estradiol and 5α-androstan-3α,17β-diol, as well as a method of finding compds. which bind to SHBG and prevent the binding of estradiol.

IT 81403-80-7

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment and prevention of prostatic disease with compds. binding to sex hormone-binding globulin (SHBG) in combinations with other compds., and method for therapeutic compound identification)

RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



L5 ANSWER 85 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1996:687311 CAPLUS

DOCUMENT NUMBER: 125:309071

ORIGINAL REFERENCE NO.: 125:57669a,57672a

TITLE: Transdermal device for the delivery of alfuzosin

INVENTOR(S): Braun, Franz-Josef

PATENT ASSIGNEE(S): Minnesota Mining and Manufacturing Co., USA

SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

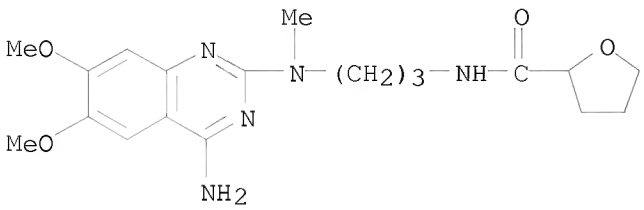
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

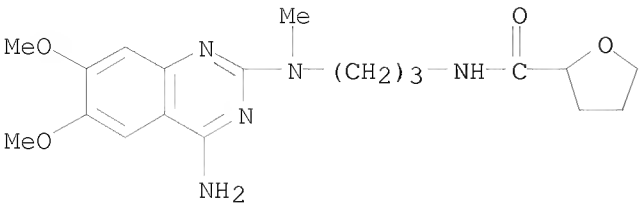
PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9630020	A1	19961003	WO 1996-US1919		19960215
W: CA, HU, JP, KR, NO					
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
CA 2215256	A1	19961003	CA 1996-2215256		19960215
EP 817633	A1	19980114	EP 1996-903816		19960215
R: CH, DE, ES, FR, GB, IT, LI, SE, IE					
HU 9802299	A2	19990201	HU 1998-2299		19960215
HU 9802299	A3	20000628			
JP 11502836	T	19990309	JP 1996-529355		19960215
NO 9704529	A	19971201	NO 1997-4529		19970930
PRIORITY APPLN. INFO.:			US 1995-414188	A	19950331
			WO 1996-US1919	W	19960215

AB A transdermal drug delivery device involves a (meth)acrylate-based adhesive copolymer, a skin penetration enhancer, and a therapeutically effective amount of alfuzosin. Lauric acid 23.3, alfuzosin 23.3, and iso-Pr myristate 6.67 g were dissolved in warm ethanol. Isooctyl acrylate-acrylamide-vinyl acetate copolymer adhesive 26.67 g were dissolved in a mixture of EtOAc and MeOH. The above two solns. were combined and mixed to provide a homogeneous coating formulation. The formulation was knife-coated on a release liner and oven-dried at 40°. The coated liner was then laminated onto a backing (1109 Scotchpack polyester film) and the laminate was die cut into patches. Penetration through hairless mouse skin was determined; cumulative amount for 48 h was 1711 μg/cm2.

IT 81403-80-7, Alfuzosin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(transdermal device for delivery of alfuzosin)
RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



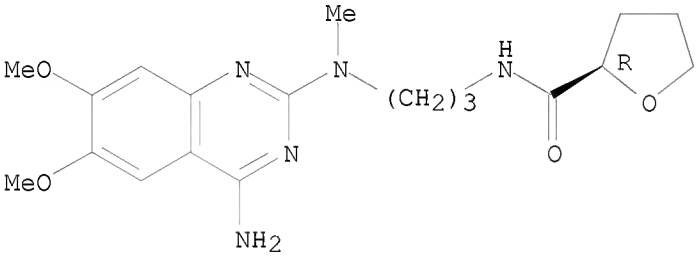
L5 ANSWER 86 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1996:595130 CAPLUS
DOCUMENT NUMBER: 126:296
ORIGINAL REFERENCE NO.: 126:47a,50a
TITLE: Transport mechanism of the α1-antagonist alfuzosin and its enantiomers in rat intestine: in vitro studies
AUTHOR(S): Haddouche, Abdenour; Boisset, Michel; Thenot, Jean-Paul; Desjeux, Jehan-Francois
CORPORATE SOURCE: Synthelabo Recherche, Departement Developpement Chimique et Pharmaceutique, Chilly-Mazarin, 91380, Fr.
SOURCE: European Journal of Pharmaceutical Sciences (1996), 4(5), 259-266
CODEN: EPSCED; ISSN: 0928-0987
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Transport of the alfuzosin and its enantiomers in rat intestine was studied in vitro, using Ussing chambers. Passage of alfuzosin was quantitated by reversed-phase HPLC or β scintillation and that of the (R)- and (S)-enantiomers by chiral chromatog. Mucosal to serosal fluxes (Jm→s) of alfuzosin decreased in the order ileum-jejunum-duodenum-colon. The concentration dependence of Jm→s was linear in the range 0.1-5 mM. Transepithelial passage of alfuzosin in ileum and colon was not polarized and transport ratio or the enantiomers in ileum and colon, was not different from 1. Depletion of cell energetics increased significantly hydro-elec. permeability and Jm→s of alfuzosin in the ileum. Apparent permeabilities of alfuzosin and D-mannitol, a paracellular probe, were strongly correlated. Sodium taurocholate, failed to increase Jm→s of D-mannitol and alfuzosin. Alfuzosin transport appears essentially passive, non enantioselective and occurs mainly through the paracellular pathway.
IT 81403-68-1, Xatral 183658-25-5 183658-26-6
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(transport mechanism of α1-antagonist alfuzosin and its enantiomers in intestine)
RN 81403-68-1 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

RN 183658-25-5 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro-, monohydrochloride, (R)- (9CI) (CA INDEX NAME)

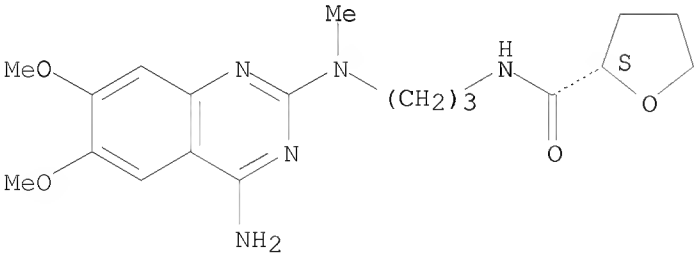
Absolute stereochemistry.



● HCl

RN 183658-26-6 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro-, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

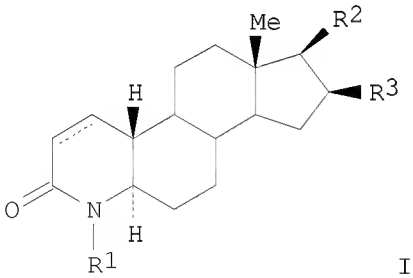


● HCl

ACCESSION NUMBER: 1996:580169 CAPLUS
DOCUMENT NUMBER: 125:212693
ORIGINAL REFERENCE NO.: 125:39531a,39534a
TITLE: 5α-Reductase-inhibiting 4-aza-19-norandrostane derivatives, their preparation, and their use, alone or with other therapeutic agents, for treatment of hyperandrogenic disorders
INVENTOR(S): Aster, Susan D.; Graham, Donald W.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9622100	A1	19960725	WO 1996-US55	19960116
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, AZ, BY, KG, KZ, RU				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2210079	A1	19960725	CA 1996-2210079	19960116
AU 9646519	A	19960807	AU 1996-46519	19960116
AU 696320	B2	19980903		
EP 804205	A1	19971105	EP 1996-902066	19960116
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
JP 10512275	T	19981124	JP 1996-522285	19960116
US 5886005	A	19990323	US 1997-817965	19970506
PRIORITY APPLN. INFO.:			US 1995-373341 A	19950117
			WO 1996-US55 W	19960116

OTHER SOURCE(S): MARPAT 125:212693
GI



I

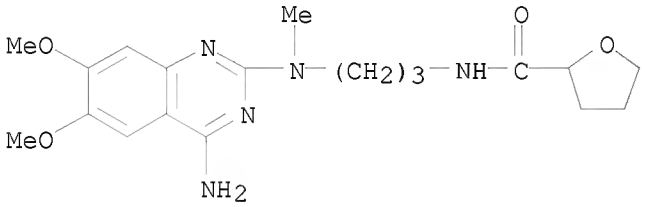
AB Compds. I [dotted line = double bond; R1 = H, Me, Et; R2 = H, (CH2)nR4, OCOR5, OCON(R5)2; R3 = OR5 when R2 is H, H when R2 is not H; R4 = CN, CON(R5)2, CO2R5; R5 = H, (substituted) C1-10 (branched) alkyl, (substituted) aryl, heteroaryl; n = 1-6] are inhibitors of 5α-reductase and are useful alone or in combination with other active agents for the treatment of hyperandrogenic disorders, e.g. acne

vulgaris, seborrhea, female hirsutism, male pattern baldness, benign prostatic hyperplasia, prostatitis, or prostatic cancer. Preparation of selected I is included.

IT 81403-80-7, Alfuzosin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(azanorandrostane derivative preparation, and their use, alone or with other therapeutic agents, for inhibiting 5α-reductase and treatment of hyperandrogenic disorders)

RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



L5 ANSWER 88 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1996:435300 CAPLUS

DOCUMENT NUMBER: 125:104287

ORIGINAL REFERENCE NO.: 125:19231a,19234a

TITLE: Structure activity relationships of a series of buspirone analogs at alpha-1 adrenoceptors: further evidence that rat aorta alpha-1 adrenoceptors are of the alpha-1D-subtype

AUTHOR(S): Saussy, David L., Jr.; Goetz, Aaron S.; Queen, Kennedy L.; King, Holly K.; Lutz, Michael W.; Rimele, Thomas J.

CORPORATE SOURCE: Dep. Receptor Biochem., Glaxo Welcome, Inc., Research Triangle Park, NC, USA

SOURCE: Journal of Pharmacology and Experimental Therapeutics (1996), 278(1), 136-144
CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

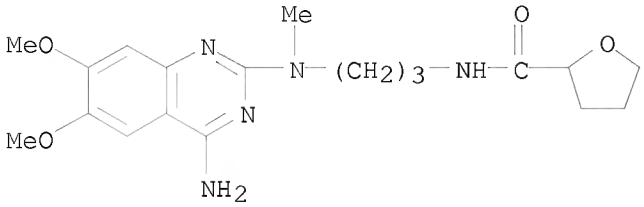
AB The activity of a series of buspirone analogs at recombinant and rat thoracic aorta alpha-1 adrenoceptors was investigated. Compound affinity for recombinant alpha-1A, alpha-1B and alpha-1D adrenoceptors from human and animal sources was determined by radioligand binding assays using membranes prepared from rat-1 fibroblasts expressing recombinant receptors with (±)-[125I]iodo-HEAT as the radioligand. Compound affinity and functional activity at rat aortic alpha-1 adrenoceptors were determined using endothelium denuded rings contracted with phenylephrine. BMY 7378 and MDL 73005EF were found to have significant selectivity for the alpha-1D-subtype and were high affinity antagonists of the alpha-1 adrenoceptors in the rat aorta. Leverage plot anal. of affinities of the buspirone analogs and a series of structurally diverse alpha-1 antagonists for recombinant alpha-1 adrenoceptors and rat aorta alpha-1 adrenoceptors demonstrate that the alpha-1 adrenoceptors in the rat aorta are predominantly of the alpha-1D subtype.

IT 81403-80-7, Alfuzosin
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL

(Biological study); PROC (Process)
(structure activity relationships of buspirone analogs at α1-adrenoceptors and characterization of rat aorta α1-adrenoceptors as α1D subtype)

RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



L5 ANSWER 89 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1996:427956 CAPLUS

DOCUMENT NUMBER: 125:132459

ORIGINAL REFERENCE NO.: 125:24537a,24540a

TITLE: Evaluation of the pharmacological selectivity profile of α1 adrenoceptor antagonists at prostatic α1 adrenoceptors: binding, functional and in vivo studies

AUTHOR(S): Kenny, B. A.; Miller, A. M.; Williamson, I. J. R.; O'Connell, J.; Chalmers, D. H.; Naylor, A. M.

CORPORATE SOURCE: Pfizer Central Res., Kent, CT13 9NJ, UK

SOURCE: British Journal of Pharmacology (1996), 118(4), 871-878
CODEN: BJPCBM; ISSN: 0007-1188

PUBLISHER: Stockton

DOCUMENT TYPE: Journal

LANGUAGE: English

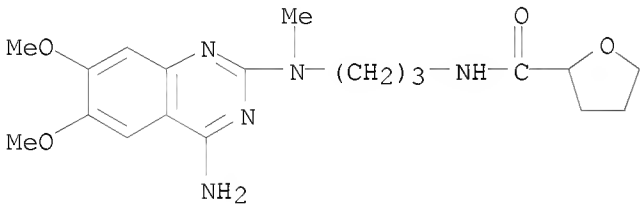
AB The profile of a range of α1 adrenoceptor antagonists was determined in vitro against cloned human α1A, α1B and α1D adrenoceptors and against noradrenaline-mediated contractions of rat aorta and human prostate. The in vivo profile of compds. was determined in an anesthetized dog model which allowed the simultaneous assessment of antagonist potency against phenylephrine-mediated increases in blood pressure and prostatic pressure. The quinazoline antagonists, prazosin, doxazosin and alfuzosin displayed high affinity but were nonselective for the three cloned human α1 adrenoceptors. Indoramin and SNAP 1069 showed selectivity for α1A and α1B adrenoceptors relative to the α1D subtype. Rec 15/2739, WB 4101, SL 89,0591, (+)- and (-)-tamsulosin showed selectivity for α1A and α1D adrenoceptors relative to the α1B subtype. RS 17053 showed high affinity and selectivity for α1A adrenoceptors (pKi 8.6) relative to α1B (pKi = 7.3) and α1D (pKi = 7.1) subtypes. (+)-Tamsulosin, (-)-tamsulosin, SL 89,0591, Rec 15/2739, SNAP 1069 and RS 17053 appeared to act as competitive antagonists of noradrenaline-mediated contractions of rat aorta yielding pA2 affinity ests. which were similar to binding affinities at cloned human α1D adrenoceptors. The following rank order was obtained: prazosin = (-)-tamsulosin > doxazosin > SL 89,0591 = (+)-tamsulosin > Rec 15/2739 > RS 17053 = SNAP 1069. (-)-Tamsulosin was a very potent, insurmountable antagonist of noradrenaline-mediated contractions of human prostate, yielding an approx. pA2 estimate of 9.8 at 1 nM. The corresponding (+)-enantiomer was 30 fold weaker. SL 89,0591,

SNAP 1069 and Rec 15/2739 yielded pA2 ests. which compared well with their α1A binding affinities. The affinity estimate for prazosin on human prostate was lower than the corresponding binding affinity determined at α1A adrenoceptors and RS 17053 was a very weak antagonist on human prostate (pA2 = 6.0) relative to the high affinity (pKi = 8.6) determined at cloned human α1A adrenoceptors. In the anesthetized dog, in vivo pseudo 'pA2' values showed that doxazosin, (+)- and (-)-tamsulosin inhibited phenylephrine-induced increases in prostatic and blood pressure with similar affinity, implying that these agents show little or no selectivity for prostatic responses in this model. SL 89,0591 and SNAP 1069 were moderately selective (3 and 6 fold resp.) for prostatic pressure relative to blood pressure. Rec 15/2739 was a more potent antagonist of phenylephrine-mediated increases in prostatic pressure ('pA2' = 8.74) compared to blood pressure ('pA2' = 7.51). Data in this study suggest that the α1 adrenoceptor mediating noradrenaline-induced contractions of human prostate, while having some of the characteristics of an α1A adrenoceptor, cannot be satisfactorily aligned with cloned α1A, α1B or α1D adrenoceptors. In addition, studies in the anesthetized dog have shown that agents having high affinity and selectivity for prostatic α1 adrenoceptors, particularly over the α1D subtype, appear to inhibit phenylephrine-induced increases in prostatic pressure selectively compared to blood pressure.

IT 81403-80-7, Alfuzosin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(evaluation of pharmacol. selectivity profile of α1 adrenoceptor antagonists at prostatic α1 adrenoceptors)

RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



L5 ANSWER 90 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1996:310377 CAPLUS

DOCUMENT NUMBER: 125:615

ORIGINAL REFERENCE NO.: 125:123a,126a

TITLE: Drugs for treatment of benign prostatic hyperplasia: affinity comparison at cloned α1-adrenoceptor subtypes and in human prostate

AUTHOR(S): Michel, M. C.; Gruebbel, B.; Taguchi, K.; Verfuerth, F.; Otto, T.; Kroepfl, D.

CORPORATE SOURCE: Dep. Med. Urol., Univ. Essen, Essen, Germany

SOURCE: Journal of Autonomic Pharmacology (1996), 16(1), 21-28
CODEN: JAPHDU; ISSN: 0144-1795

PUBLISHER: Blackwell

DOCUMENT TYPE: Journal

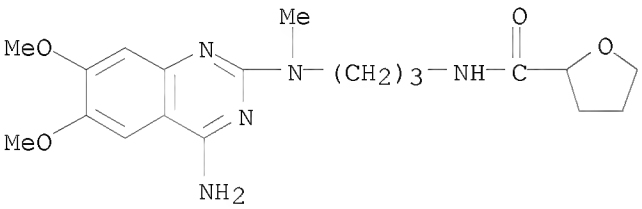
LANGUAGE: English

AB We have previously shown that among α1-adrenoceptor antagonists used or investigated for the treatment of benign prostatic hyperplasia, tamsulosin discriminates α1-adrenoceptor subtypes in rat tissues

whereas alfuzosin and naftopidil do not. We now expand these studied to addnl. drugs (doxazosin, terazosin) being used and/or investigated for this purpose, and have evaluated all of these drugs at cloned subtypes and in human prostate. Competition binding studies were performed with [3H]-prazosin in membrane samples from rat spleen, kidney and cerebral cortex and human prostate and with cloned α1-adrenoceptors expressed in COS cells. Doxazosin and terazosin did not discriminate α1-adrenoceptor subtypes in rat kidney and cerebral cortex. In contrast, the subtype present in the tissues were well discriminated by the α1A-adrenoceptor-selective reference drug WB 4101. Alfuzosin, doxazosin, naftopidil and terazosin did not discriminate cloned α1-adrenoceptor subtypes transiently expressed in COS cells whereas tamsulosin and WB 4101 did. In human prostate, alfuzosin, doxazosin, naftopidil and terazosin did not discriminate the α1-adrenoceptor subtypes present in this tissue whereas tamsulosin and the α1A-adrenoceptor-selective reference drugs WB 4101, phentolamine and 5-methylurapidil did. Based on data with the α1A-adrenoceptor-selective drugs, human prostate contains α1A- and α1B-adrenoceptors in an approx. 70:30% ratio. We conclude that tamsulosin, in common with WB 4101, but in contrast to alfuzosin, doxazosin, naftopidil, and terazosin is selective for α1A-adrenoceptors which appear to dominate in the human prostate; the therapeutic relevance of this selectivity remains to be assessed in clin. studies.

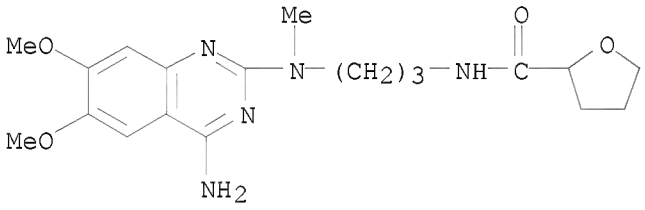
IT 81403-80-7, Alfuzosin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drugs for treatment of benign prostatic hyperplasia in relation to affinity comparison at cloned α1-adrenoceptor subtypes and in human prostate)

RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



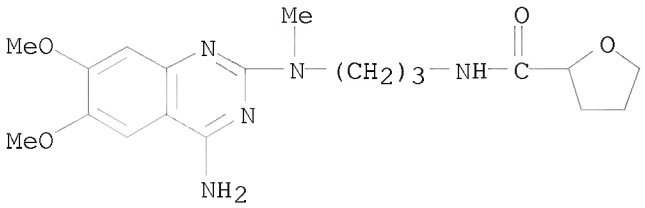
L5 ANSWER 91 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1996:255306 CAPLUS
DOCUMENT NUMBER: 125:986
ORIGINAL REFERENCE NO.: 125:215a,218a
TITLE: Effect on intravenous alfuzosin on urethral pressure in patients with neurogenic bladder dysfunction
AUTHOR(S): Perrigot, Michel; Delauche-Cavallier, Marie C.; Amarenco, Gerard; Geffriaud, Christine; Stalla-Bourdillon, Aline; Costa, Pierre
CORPORATE SOURCE: Neurological Rehabilitation Unit, Hosp. Pitie-Salpetriere, Paris, 75651, Fr.
SOURCE: Neurourology and Urodynamics (1996), 15(2), 119-31
CODEN: NEUREM; ISSN: 0733-2467
PUBLISHER: Wiley-Liss

DOCUMENT TYPE: Journal
LANGUAGE: English
AB In order to assess the ability of a single i.v. (IV) injection of alfuzosin, a selective alpha-1 blocker, in reducing high urethral tone in patients with symptomatic neurogenic bladder dysfunction (NBD), 163 patients (mean maximal urethral pressure [MUP] 108 ± 46 cm H2O) were enrolled in a double-blind, placebo-controlled, parallel-group trial and were randomly allocated to receive 0.5 mg (n = 45), 1 mg (n = 41), 2 mg (n = 39) alfuzosin or placebo (n = 38). The decrease in MUP was dose-dependent and statistically significant (P ≤ 0.05) for 1 and 2 mg alfuzosin (resp., 43 ± 28 cm H2O and 46 ± 27 cm H2O decreases vs. baseline) in comparison with placebo (23 ± 30 cm H2O). The 2 mg dose level was the most effective leading to a .vphi.30 or 50% decrease in MUP in, resp., 69 and 44% of patients. The safety of all three alfuzosin dose levels was satisfactory and comparable to placebo. IV alfuzosin induces, in a dose-related manner,a clin. significant decrease in urethral pressure in patients with NBD and high urethral tone, and may be safely used as a pharmacol. test as part of an urodynamic investigation.
IT 81403-80-7, Alfuzosin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect on i.v. alfuzosin on urethral pressure in humans with neurogenic bladder dysfunction)
RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)

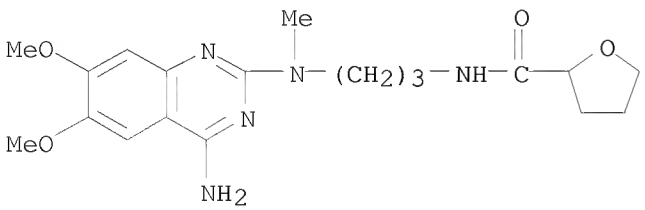


L5 ANSWER 92 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1996:126566 CAPLUS
DOCUMENT NUMBER: 124:249470
ORIGINAL REFERENCE NO.: 124:45861a,45864a
TITLE: Benign prostate hyperplasia. Rational therapy of BPH with new active substances
AUTHOR(S): Brom, Stefan
CORPORATE SOURCE: Apotheke, Klin. Grosshadern, Munich, D-81377, Germany
SOURCE: Deutsche Apotheker Zeitung (1996), 136(8), 29-32, 35-6
CODEN: DAZEA2; ISSN: 0011-9857
PUBLISHER: Deutscher Apotheker Verlag
DOCUMENT TYPE: Journal; General Review
LANGUAGE: German
AB A review with 31 refs., on benign prostate hyperplasia (BPH) and the treatment with Alfuzosin, Terazosin, Finasteride, and phytopharmaceuticals (Urticae radix, Sabal fructus, and Cucurbutae peponis semen), including pharmacokinetics.
IT 81403-80-7, Alfuzosin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(rational therapy of benign prostate hyperplasia)
RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



L5 ANSWER 93 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1995:933668 CAPLUS
DOCUMENT NUMBER: 124:685
ORIGINAL REFERENCE NO.: 124:147a,150a
TITLE: Effects of alfuzosin on urethral and blood pressures in conscious male rats
AUTHOR(S): Martin, Denis; Jammes, Dominique; Angel, Itzchak
CORPORATE SOURCE: Dep. Int. Med., Synthelabo Recherche, Rueil-Malmaison, 92504, Fr.
SOURCE: Life Sciences (1995), 57(25), PL387-PL391
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This study was undertaken to determine simultaneously the effects of Alfuzosin on urethral and blood pressures in the same conscious male rat. Alfuzosin (i.v., 3, 10 and 30 μg/kg) dose-dependently decreased urethral pressure without affecting mean arterial blood pressure. At the higher dose, blood pressure was only slightly and transiently decreased while a marked decrease (-40%) in urethral pressure was observed Therefore, this exptl. model is suitable to assess uroselectivity.
IT 81403-80-7, Alfuzosin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alfuzosin effect on urethral and blood pressures in conscious male rats in relation to exptl. model for uroselectivity assessment)
RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



L5 ANSWER 94 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1995:922027 CAPLUS

DOCUMENT NUMBER: 123:322110
ORIGINAL REFERENCE NO.: 123:57561a,57564a
TITLE: Sustained-release pharmaceutical dosage forms containing alfuzosin hydrochloride
INVENTOR(S): Andrieu, Veronique; Montel, Jean; Wick, Alexander
PATENT ASSIGNEE(S): Synthelabo S. A., Fr.
SOURCE: Eur. Pat. Appl., 8 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

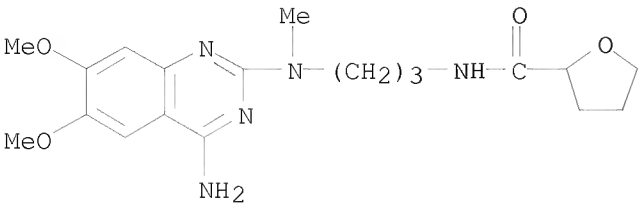
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 673650	A1	19950927	EP 1995-400521	19950313
EP 673650	B1	20010801		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
FR 2717388	A1	19950922	FR 1994-3257	19940321
FR 2717388	B1	19961122		
AT 203672	T	20010815	AT 1995-400521	19950313
CA 2144917	A1	19950922	CA 1995-2144917	19950317
FI 9501300	A	19950922	FI 1995-1300	19950320
NO 9501055	A	19950922	NO 1995-1055	19950320
NO 307813	B1	20000605		
AU 9514955	A	19950928	AU 1995-14955	19950320
AU 681236	B2	19970821		
JP 07258085	A	19951009	JP 1995-60506	19950320
ZA 9502290	A	19960124	ZA 1995-2290	19950320
CN 1116524	A	19960214	CN 1995-104072	19950320
HU 72635	A2	19960528	HU 1995-818	19950320
US 5589190	A	19961231	US 1995-406405	19950320
IL 113053	A	19991222	IL 1995-113053	19950320
PRIORITY APPLN. INFO.:			FR 1994-3257 A	19940321

AB Sustained-release pharmaceutical dosage forms comprise a core containing alfuzosin hydrochloride (I) and a pH-dependent coating compns. Tablets containing I 3.3, lactose 69.4, microcryst. cellulose 17.8, PVP 5.0, sodium carboxymethyl starch 4.0, Mg stearate 0.5% were coated with a composition comprising methacrylic acid copolymer 75.7, diacetylmonoglcerides 7.5, and talc 16.8%. The release of I from tablet after 3 h was 100%.

IT 81403-68-1, Alfuzosin hydrochloride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sustained-release pharmaceutical dosage forms containing alfuzosin hydrochloride)

RN 81403-68-1 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

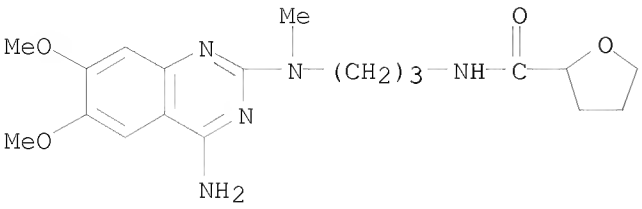
L5 ANSWER 95 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1995:909424 CAPLUS
DOCUMENT NUMBER: 123:314006
ORIGINAL REFERENCE NO.: 123:56295a,56298a
TITLE: Preparation of alfuzosin hydrochloride dihydrate
INVENTOR(S): Borrega, Regis; Kitamura, Satoshi
PATENT ASSIGNEE(S): Synthelabo S. A., Fr.
SOURCE: Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 663398	A1	19950719	EP 1994-120539	19941223
EP 663398	B1	20000315		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 07206857	A	19950808	JP 1993-353828	19931228
AT 190614	T	20000415	AT 1994-120539	19941223
US 5545738	A	19960813	US 1994-364180	19941227
PRIORITY APPLN. INFO.:			JP 1993-353828 A	19931228

AB Alfuzosin hydrochloride dihydrate, the most stable crystal-hydrate form of alfuzosin hydrochloride, is prepared by heating anhydrous alfuzosin hydrochloride in a 4:1 acetone-water solvent mixture at approx. 60° and cooling the solution until the dihydrate ppts. out. Numerous X-ray powder diffraction patterns of the various alfuzosin hydrochloride crystal hydrates are presented as well as data demonstrating the absorption of atmospheric water and the concomitant interchange of various alfuzosin hydrochloride crystal-hydrate states.

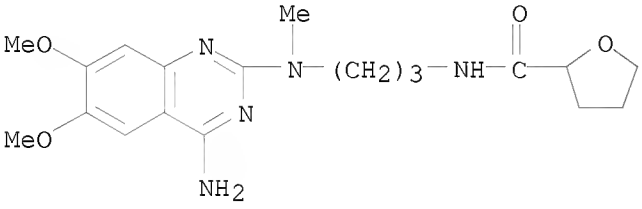
IT 81403-68-1, Alfuzosin hydrochloride 170103-16-9
170103-17-0
RL: PRP (Properties)
(preparation of alfuzosin hydrochloride dihydrate)

RN 81403-68-1 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

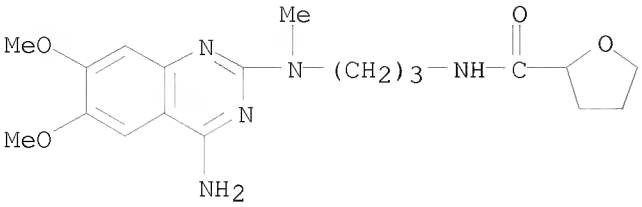
RN 170103-16-9 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro-, hydrochloride, hydrate (1:1:3) (CA INDEX NAME)



● HCl

● 3 H_2O

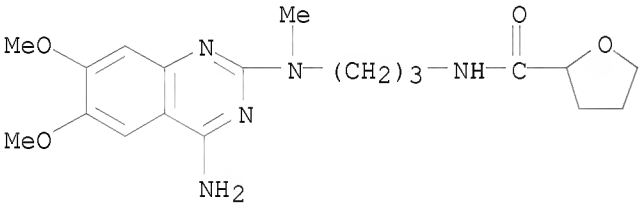
RN 170103-17-0 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro-, hydrochloride, hydrate (1:1:4) (CA INDEX NAME)



● HCl

● 4 H_2O

IT 170103-15-8P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation of alfuzosin hydrochloride dihydrate)
RN 170103-15-8 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro-, hydrochloride, hydrate (1:1:2) (CA INDEX NAME)



● HCl

● 2 H_2O

L5 ANSWER 96 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1995:723465 CAPLUS
DOCUMENT NUMBER: 123:102804
ORIGINAL REFERENCE NO.: 123:18034h
TITLE: The use of alfuzosin or terazosin in the treatment of premature ejaculation
INVENTOR(S): Cavallini, Giorgio
PATENT ASSIGNEE(S): Italy
SOURCE: PCT Int. Appl., 11 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

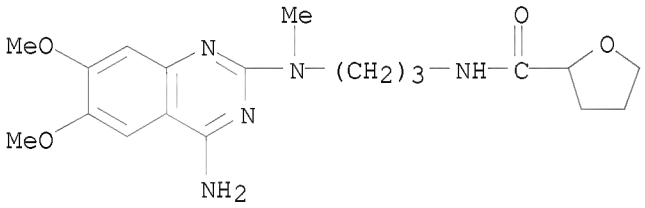
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9513072	A1	19950518	WO 1994-EP3661	19941108
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 728000	A1	19960828	EP 1994-931582	19941108
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 09504798	T	19970513	JP 1995-513583	19941108
US 5707999	A	19980113	US 1996-624603	19960416
PRIORITY APPLN. INFO.:			IT 1993-MI2412 A	19931112
			WO 1994-EP3661 W	19941108

AB Use of α1-blockers, alfuzosin and terazosin in the treatment of premature ejaculation is disclosed. Clin. evaluations proved that alfuzosin and terazosin were effective in the treatment of psychogenic premature ejaculation, particularly in patients resistant to psychotherapy.

IT 81403-80-7, Alfuzosin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alfuzosin or terazosin for treatment of psychogenic premature ejaculation)

RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



L5 ANSWER 97 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1995:316190 CAPLUS

DOCUMENT NUMBER: 122:89486

ORIGINAL REFERENCE NO.: 122:16779a,16782a

TITLE: A drug delivery composition for alpha-adrenoreceptor blocking agents

INVENTOR(S): Illum, Lisbeth; Watts, Peter; Farraj, Nidal

PATENT ASSIGNEE(S): Danbiosyst UK Ltd., UK

SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9427582	A1	19941208	WO 1994-GB1158	19940527
W: AU, CA, FI, GB, JP, NO, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2163340	A1	19941208	CA 1994-2163340	19940527
AU 9468020	A	19941220	AU 1994-68020	19940527
AU 684786	B2	19980108		

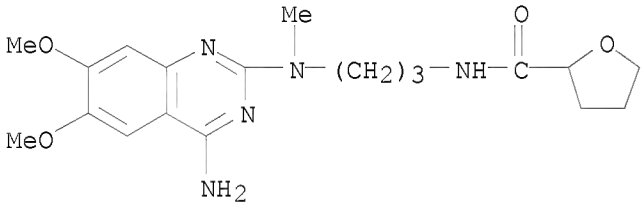
GB 2292315	A	19960221	GB 1995-23191	19940527
GB 2292315	B	19970402		
EP 700285	A1	19960313	EP 1994-916318	19940527
EP 700285	B1	19980923		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, NL, PT, SE				
JP 09504779	T	19970513	JP 1994-500403	19940527
AT 171370	T	19981015	AT 1994-916318	19940527
ES 2124889	T3	19990216	ES 1994-916318	19940527
NO 9504583	A	19951114	NO 1995-4583	19951114
NO 306759	B1	19991220		
FI 9505730	A	19960126	FI 1995-5730	19951128
PRIORITY APPLN. INFO.:			GB 1993-11191 A	19930529
			WO 1994-GB1158 W	19940527

AB An oral drug delivery composition for α-adrenoreceptor blockers with two phase release profile (release in the upper gastrointestinal tract and sustained release in the terminal ileum and/or the colon) comprises a controlled release system such as a hydrophilic gel matrix. The specific release of the second portion of the drug in the colon can be achieved by coating tablets containing the second portion with a pH or redox sensitive coating such as a poly(Me methacrylate). A controlled-release system was devised comprising three tablets, each containing alfuzosin-HCl 3.0, Methocel K 100M 15.0, Avicel 23.0, Emcompress 107.5, and Mg stearate 1.5 mg, resp.; two of three tablets contained an enteric coating of Eudragit L100 and Eudragit S100, designed to delay drug release until the terminal ileum or colon region is reached; tablets were designed to fit inside a size 0 hard gelatin capsules.

IT 81403-68-1, Alfuzosin hydrochloride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlled-release delivery system for α-adrenergic blockers)

RN 81403-68-1 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

L5 ANSWER 98 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN

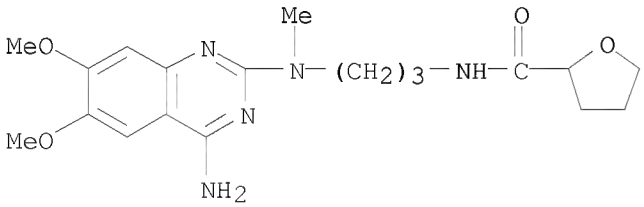
ACCESSION NUMBER:	1995:300497 CAPLUS
DOCUMENT NUMBER:	122:96453
ORIGINAL REFERENCE NO.:	122:18011a,18014a
TITLE:	Use of recombinant α1-adrenoceptors to characterize subtype selectivity of drugs for the treatment of prostatic hypertrophy
AUTHOR(S):	Foglar, Rudolf; Shibata, Katsushi; Horie, Kuniko; Hirasawa, Akira; Tsujimoto, Gozoh
CORPORATE SOURCE:	Department of Molecular and Cellular Pharmacology, National Children's Medical Research Center, 3-35-31

Taishido, Setagaya-ku, Tokyo, 154, Japan
SOURCE: European Journal of Pharmacology, Molecular Pharmacology Section (1995), 288(2), 201-7
CODEN: EJPPET; ISSN: 0922-4106
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Several α1-adrenoceptor antagonists have recently been developed for the treatment of benign prostatic hypertrophy because of their less frequent systemic side-effects compared to conventional α1-adrenoceptor blockers. One potential explanation for their good tolerability would be the selectivity for a certain subtype of α1-adrenoceptor. Utilizing COS-7 cells expressing the rat α1A, the hamster α1B and the human α1C-adrenoceptors, the authors investigated affinities of alfuzosin, doxazosin, terazosin, indoramin and (+)- and (-)-5-[2-[[2-(o-ethoxyphenoxy)ethyl] amino]propyl]-2-methoxybenzesulfonamide HCl (YM 617) compared to prazosin. Radioligand binding studies showed that the affinities of α1-adrenoceptor subtypes for alfuzosin (Ki value; α1A: 2.4 nM, α1B: 1.4 nM, α1C: 4.2 nM), doxazosin (Ki value; α1A: 2.7 nM, α1B: 3.2 nM, α1C: 7.5 nM), terazosin (Ki value; α1A: 2.5 nM, α1B: 2.7 nM, α1C: 7.1 nM), indoramin (Ki value; α1A: 69 nM, α1B: 21 nM, α1C: 13 nM) and prazosin (Ki value; α1A: 0.16 nM, α1B: 0.19 nM, α1C: 0.2 nM) were equipotent to the three receptor subtypes. Unlike these antagonists, both (+)- and (-)-YM617 had relatively lower affinity for α1B receptors compared to the other subtypes (Ki value; for (+)-YM617, α1A: 22 nM, α1B: 96 nM, α1C: 4.3 nM; for (-)-YM617, α1A: 0.11 nM, α1B: 0.7 nM, α1C: 0.035 nM). The data suggest that α1-adrenoceptor antagonists currently used for the treatment of the benign prostatic hyperplasia do not show substantial subtype selectivity.

IT 81403-80-7, Alfuzosin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of recombinant α1-adrenoceptors to characterize subtype selectivity of drugs for treatment of prostatic hypertrophy)

RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



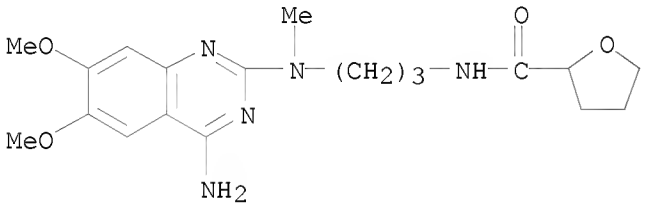
L5 ANSWER 99 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1995:216252 CAPLUS
DOCUMENT NUMBER: 122:196
ORIGINAL REFERENCE NO.: 122:31a,34a
TITLE: Determination of alfuzosin in human plasma by high-performance liquid chromatography with column-switching

AUTHOR(S): Carlucci, Giuseppe; Di Giuseppe, Enrico; Mazzeo, Piertro
CORPORATE SOURCE: Dip. Chim., Univ. dell'Aquila, LAquila, Italy
SOURCE: Journal of Liquid Chromatography (1994), 17(18), 3989-97
CODEN: JLCHD8; ISSN: 0148-3919
PUBLISHER: Dekker
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A high-performance liquid chromatog. method for the determination of alfuzosin in human plasma has been developed and validated. A column-switching procedure without extraction was used to isolate the drug from biol. matrix prior to the quant. anal. The lower limit of detection for the analyte was 1 ng/mL. The method was linear from 2 to 150 ng/mL for human plasma. Within- and between-assay precision and accuracy were all found to be <5.2% at the eight concns. evaluated. This procedure, simple and rapid, is suitable for pharmacol. studies on alfuzosin.

IT 81403-80-7, Alfuzosin
RL: ANT (Analyte); ANST (Analytical study)
(alfuzosin determination in human plasma by HPLC)

RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



L5 ANSWER 100 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1994:315765 CAPLUS
DOCUMENT NUMBER: 120:315765
ORIGINAL REFERENCE NO.: 120:55277a,55280a
TITLE: α1-Adrenoceptor subtype affinities of drugs for the treatment of prostatic hypertrophy. Evidence for heterogeneity of chloroethylclonidine-resistant rat renal α1-adrenoceptor
AUTHOR(S): Michel, Martin C.; Buescher, Rainer; Kerker, Jens; Kraneis, Henner; Erdbruegger, Wilhelm; Brodde, Otto Erich
CORPORATE SOURCE: Dep. Med., Univ. Essen, Essen, D-45122D-45122, Germany
SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology (1993), 348(4), 385-95
CODEN: NSAPCC; ISSN: 0028-1298
DOCUMENT TYPE: Journal
LANGUAGE: English

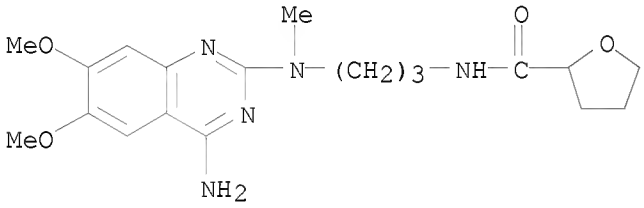
AB The authors have used radioligand binding and inositol phosphate accumulation studies to determine the affinity at mixed α1A- and α1B-adrenoceptors (rat cerebral cortex and kidney), α1A-adrenoceptors (rat cerebral cortex and kidney following inactivation of α1B-adrenoceptors by chloroethylclonidine treatment) and α1B-adrenoceptors (rat spleen) for drugs currently under investigation for the treatment of benign prostatic hypertrophy,

alfuzosin, naftopidil and (-)- and (+)-tamsulosin. Alfuzosin and naftopidil had similar affinities in all model systems (approx. 10 nM and 130 nM, resp.) and lacked relevant selectivity for α1-adrenoceptor subtypes. Their potency to inhibit noradrenaline-stimulated inositol phosphate formation in cerebral cortex matched their affinities as determined in the binding studies. Tamsulosin had higher affinity at α1A- than at α1B-adrenoceptors, and was slightly more potent than alfuzosin and naftopidil at α1B- and considerably more potent at α1A-adrenoceptors. However, the interaction of the tamsulosin isomers with chloroethylclonidine-insensitive adrenoceptors (α1A-like) was complex. A detailed anal. of the tamsulosin data and those obtained with other drugs, most notably noradrenaline and oxymetazoline, suggested that chloroethylclonidine-insensitive α1-adrenoceptors may be heterogeneous and that this heterogeneity may differ between cerebral cortex and kidney of the rat.

IT 81403-80-7, Alfuzosin
RL: BIOL (Biological study)
(α1-adrenoceptor subtype affinity of)

RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



L5 ANSWER 101 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1994:290579 CAPLUS

DOCUMENT NUMBER: 120:290579

ORIGINAL REFERENCE NO.: 120:50995a,50998a

TITLE: The α1-adrenergic receptor that mediates smooth muscle contraction in human prostate has the pharmacological properties of the cloned human α1c subtype

AUTHOR(S): Forray, Carlos; Bard, Jonathan A.; Wetzel, John M.; Chiu, George; Shapiro, Ellen; Tang, Rui; Lepor, Herbert; Hartig, Paul R.; Weinshank, Richard L.; et al.

CORPORATE SOURCE: Synaptic Pharm. Corp., Paramus, NJ, 07652, USA

SOURCE: Molecular Pharmacology (1994), 45(4), 703-8
CODEN: MOPMA3; ISSN: 0026-895X

DOCUMENT TYPE: Journal

LANGUAGE: English

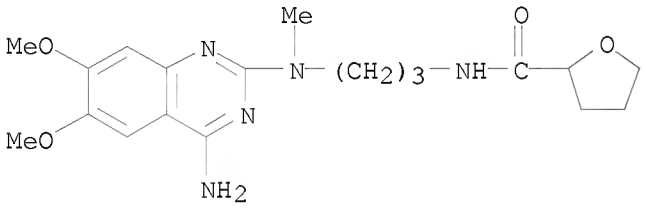
AB Mol. cloning studies have revealed the existence of three subtypes of α1-adrenergic receptors. However, the link between any individual subtype and its functional role in the body has remained elusive. In an effort to bridge the gap between mol. biol. and pathophysiol., the authors have chosen a model smooth muscle system, the human prostate, and investigated the role of α1 subtypes in this tissue. To determine which α1-adrenergic receptor subtype mediates the contractile response of the human prostate, the authors first studied the pharmacol. properties of three cloned human α1 subtypes (α1a/d, α1b, and α1c). Prazosin, terazosin, doxazosin, alfuzosin, and abanoquil

showed no selectivity for the human α1 subtypes. WB-4101 and 5-methylurapidil showed a rank order of potency of α1c > α1a/d » α1b. Indoramin and (+)-niguldipine were selective for the α1c-adrenergic receptor, with at least 10-fold lower affinity at either α1a/d or α1b subtypes. SK&F104856 was 6-fold more potent at the α1/d receptor subtype than at α1b- or α1c-adrenergic receptors. The authors next determined the potency of these antagonists to inhibit the phenylephrine-induced contraction of human prostatic tissue in vitro. The potencies of indoramin, 5-methylurapidil, and SK&F104856 to inhibit the contractile response and to displace [3H]prazosin from the cloned human α1c subtype were similar. The authors' data suggest that the α1 receptor that mediates the contraction of human prostate smooth muscle has the pharmacol. properties of the cloned human α1c-adrenergic receptor. The findings of the present study suggest that selective α1c-adrenergic receptor antagonists may be clin. more efficacious and better tolerated agents for the treatment of symptomatic benign prostatic hyperplasia.

IT 81403-80-7, Alfuzosin
RL: BIOL (Biological study)
(α1-adrenergic receptor subtype selectivity of)

RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



L5 ANSWER 102 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1994:207833 CAPLUS

DOCUMENT NUMBER: 120:207833

ORIGINAL REFERENCE NO.: 120:36517a,36520a

TITLE: The effect of cimetidine on the pharmacokinetics of single oral doses of alfuzosin

AUTHOR(S): Desager, J. P.; Harvengt, C.; Bianchetti, G.; Rosenzweig, P.

CORPORATE SOURCE: Fac. Med., Univ. Cathol. Louvain, Brussels, Belg.

SOURCE: International Journal of Clinical Pharmacology, Therapy and Toxicology (1993), 31(11), 568-71
CODEN: IJCPB5; ISSN: 0300-9718

DOCUMENT TYPE: Journal

LANGUAGE: English

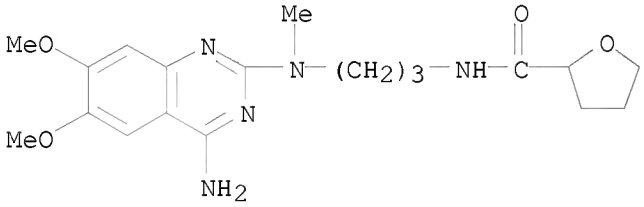
AB Alfuzosin is a new α1-adrenoceptor antagonist particularly effective in the symptomatic treatment of benign prostatic hypertrophy (BPH). The elimination of alfuzosin being almost entirely metabolic, the potential pharmacokinetic interaction with cimetidine (H2-receptor antagonist) was investigated in 10 healthy young subjects. Pharmacokinetics of alfuzosin were appraised as a 5 mg oral dose before, after one day and after 20 days of cimetidine (1 g/d) administration. An inhibition of the hepatic mixed function oxidase system by cimetidine was established by the oral antipyrine clearance test. Under these conditions, alfuzosin pharmacokinetics were only marginally affected by concomitant cimetidine

administration. Surprisingly, a significantly shorter elimination half-life was found after 20 days on cimetidine (from 5.1 ± 0.4 h to 4.4 ± 0.5 h). This fact must be attributed to the large inter-individual variation in pharmacokinetic parameters reported for alfuzosin. Cmax and AUC increased up to 20% after cimetidine but without statistical significance. No side-effects on the association cimetidine-alfuzosin were reported. In conclusion, there is a lack of pharmacokinetic interaction on cimetidine-alfuzosin co-administration.

IT 81403-80-7, Alfuzosin
RL: PROC (Process)
(interactions of, with cimetidine pharmacokinetics of, in humans)

RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



L5 ANSWER 103 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1994:152922 CAPLUS

DOCUMENT NUMBER: 120:152922

ORIGINAL REFERENCE NO.: 120:26636h,26637a

TITLE: Alfuzosin: a comparison of the steady-state pharmacokinetics of two dosages in middle-aged and elderly healthy male volunteers

AUTHOR(S): Crome, P.; Wijawardhana, P.; Ankier, S.I.; Curson, V.H.; Thenot, J.P.; Bianchetti, G.

CORPORATE SOURCE: Dep. Health Care Elderly, Orpington Hosp., Orpington/Kent, UK

SOURCE: Drug Investigation (1993), 6(3), 156-61
CODEN: DRUIEA; ISSN: 0114-2402

DOCUMENT TYPE: Journal

LANGUAGE: English

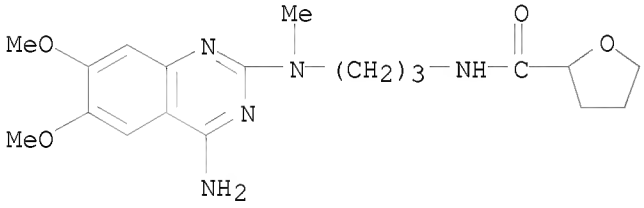
AB The steady-state pharmacokinetics and tolerability of the α1-adrenoceptor antagonist alfuzosin were investigated in 12 healthy male volunteers aged 50 to 70 yr using an open crossover design. Comparison of the pharmacokinetic profile in subjects receiving repeated doses of either 7.5 or 10 mg/day for 5 days did not reveal any differences except those related to the dose administered. The times to peak plasma concns. (tmax) were not significantly different after sequence A (2.5mg at 0800, 1400 and 2000h) or sequence B (2.5mg at 0800, 1400 and 5mg at 2000h). The mean (± SEM) tmax after the 3 doses on day 5 were: treatment A, 2.0 ± 0.2, 1.4 ± 0.1 and 2.3 ± 0.3h, and treatment B, 1.9 ± 0.1, 1.9 ± 0.2 and 1.8 ± 0.2h. Peak concns. following the first two 2.5mg doses, identical in both treatment sequences, were also not significantly different: treatment A, 10.4 ± 0.7 and 12.0 ± 0.9 μg/L, treatment B, 11.5 ± 0.9 and 11.4 ± 0.8 μg/L (mean ± SEM). Cmax following the 2000h dose was significantly different ($p = 0.0004$) and in direct proportion to the larger dose: treatment A, 13.9 ± 1.0 μg/L; treatment B, 22.6 ± 1.7 μg/L (mean ± SEM). Similarly, the area under the plasma concentration-time curve (AUC) was significantly ($p = 0.0001$) greater with the larger dose: treatment A, 184

± 13 and treatment B, 244 ± 19 μg/L/h (mean ± SEM). The ratio of the AUC values obtained following treatments A and B was 77.9 ± 2.5%, which corresponds to the ratio between the total dosages of treatments A and B, i.e. 75%. Five of the 12 subjects who completed the study reported one adverse event each. Three subjects reported headache, one subject experienced dizziness when standing on 2 occasions, and another subject reported experiencing dry mouth. All adverse events resolved without treatment. Comparison of the 2 dosage regimens did not reveal any significant differences relating to hemodynamic parameters.

IT 81403-80-7, Alfuzosin
RL: PROC (Process)
(steady-state pharmacokinetics of, in middle-aged and elderly men)

RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



L5 ANSWER 104 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1994:45870 CAPLUS

DOCUMENT NUMBER: 120:45870

ORIGINAL REFERENCE NO.: 120:8207a,8210a

TITLE: Alfuzosin, a selective α1-adrenoceptor antagonist in the lower urinary tract

AUTHOR(S): Lefevre-Borg, F.; O'Connor, S. E.; Schoemaker, H.; Hicks, P. E.; Lechaire, J.; Gautier, E.; Pierre, F.; Pimoule, C.; Manoury, P.; Langer, S. Z.

CORPORATE SOURCE: Dep. Biol., Synthelabo Rech., Bagneux, 92225, Fr.

SOURCE: British Journal of Pharmacology (1993), 109(4), 1282-9
CODEN: BJPCBM; ISSN: 0007-1188

DOCUMENT TYPE: Journal

LANGUAGE: English

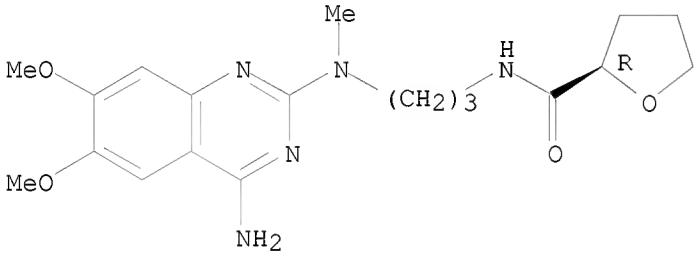
AB Phenylephrine-induced contractions of rabbit isolated trigone and urethra were antagonized in a competitive manner by alfuzosin (pA2 7.44 and 7.30, resp.) and prazosin. The characteristics of [3H]-prazosin binding to human prostatic adenoma tissue were evaluated. [3H]-prazosin was potently displaced by α1-adrenoceptor specific agents including alfuzosin, its (+)- and (-)-enantiomers and prazosin, but only weakly by α2-adrenoceptor selective agents, for example, yohimbine. In the pithed rat, alfuzosin (0.03-0.3 mg kg-1, i.v.) markedly inhibited pressor responses produced by the α1-selective agonist, cirazoline but inhibited only slightly responses to the α2-selective agonist, UK 14,304. Alfuzosin (1 mg kg-1, i.v.) had minimal effects against responses mediated by stimulation of prejunctional α2-receptors (UK 14,304-induced inhibition of sympathetic tachycardia). In the anesthetized cat, alfuzosin (0.001-1 mg kg-1, i.v.) and prazosin (0.001-0.3 mg kg-1, i.v.) produced dose-related inhibition of the increases in urethral pressure caused by stimulation of sympathetic hypogastric nerves. Prazosin was approx. 5 fold more potent than alfuzosin. When phenylephrine was employed to induce urethral and vascular α1-mediated tone simultaneously, prazosin inhibited both

stimuli with similar potency whereas alfuzosin was 3-5 fold more potent against elevated urethral pressure. This functional uroselectivity of alfuzosin was more evident by the intraduodenal route, since doses of 0.03 and 0.1 mg kg-1 alfuzosin inhibited urethral pressure with minimal effects on arterial blood pressure. Alfuzosin is a potent selective α1-adrenoceptor antagonist in tissues of the lower urinary tract including the human prostate. This provides a pharmacol. basis for its use in the treatment of benign prostatic hypertrophy.

IT 123739-69-5 123739-70-8
RL: BIOL (Biological study)
(α1-adrenergic antagonist, in human and laboratory animal lower urinary tract)

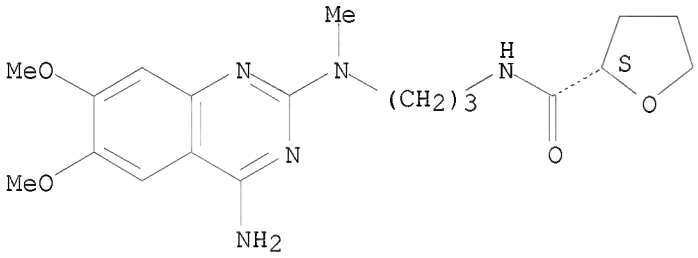
RN 123739-69-5 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



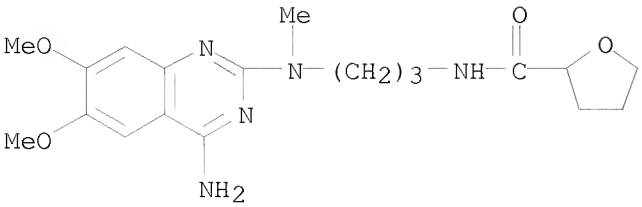
RN 123739-70-8 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 81403-80-7, Alfuzosin
RL: BIOL (Biological study)
(α1-adrenergic antagonist, in human and laboratory animal lower urinary tract, benign prostatic hypertrophy-related urinary obstruction treatment in relation to)

RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



L5 ANSWER 105 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1993:678780 CAPLUS
DOCUMENT NUMBER: 119:278780
ORIGINAL REFERENCE NO.: 119:49719a,49722a
TITLE: Pharmaceutical compositions containing 5-α-reductase inhibitors and α-adrenergic receptor antagonists for treatment of benign prostatic hypertrophy
INVENTOR(S): Hieble, Jacob Paul; Metcalf, Brian Walter
PATENT ASSIGNEE(S): SmithKline Beckman Corp., USA
SOURCE: PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

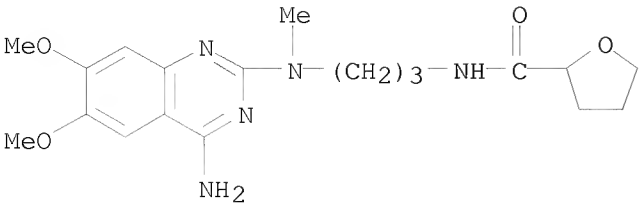
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9319758	A1	19931014	WO 1993-US3145	19930402
W: AU, CA, JP, KR, NZ, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
ZA 9302355	A	19941003	ZA 1993-2355	19930401
AU 9339451	A	19931108	AU 1993-39451	19930402
AU 668157	B2	19960426		
EP 633781	A1	19950118	EP 1993-908738	19930402
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 07505398	T	19950615	JP 1993-517741	19930402
PRIORITY APPLN. INFO.:			US 1992-862117 A1	19920402
			US 1992-997792 A1	19921229
			WO 1993-US3145 A	19930402

AB Pharmaceutical compns. containing 5-α-reductase inhibitors, e.g. N-butyl-androst-3,5-diene-17β-carboxamide-3-carboxylic acid (I) and α-adrenergic receptor antagonists, e.g. terazocin (II), are used for treatment of benign prostatic hypertrophy. A tablet contained I 50, II 50, Mg stearate 10, and lactose 150mg.

IT 81403-80-7D, Alfuzosin, mixts. with 5-α-reductase inhibitors
151651-05-7
RL: BIOL (Biological study)
(pharmaceutical compns. containing, for treatment of benign prostatic hypertrophy)

RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)

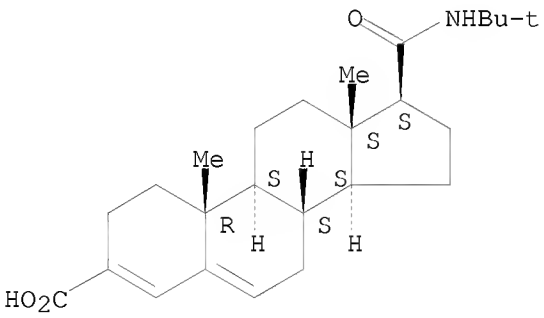


RN 151651-05-7 CAPLUS
CN Androsta-3,5-diene-3-carboxylic acid, 17-[[(1,1-dimethylethyl)amino]carbonyl]-, (17β)-, mixt. with N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro-2-furancarboxamide (9CI) (CA INDEX NAME)

CM 1

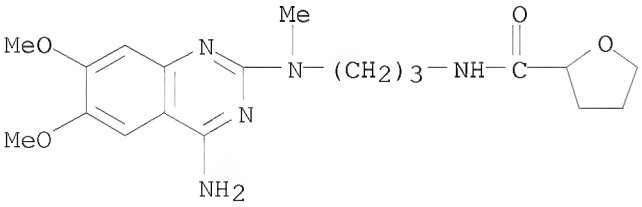
CRN 119169-78-7
CMF C25 H37 N O3

Absolute stereochemistry.



CM 2

CRN 81403-80-7
CMF C19 H27 N5 O4



L5 ANSWER 106 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1993:823 CAPLUS
DOCUMENT NUMBER: 118:823
ORIGINAL REFERENCE NO.: 118:171a,174a
TITLE: Adrenergic agonists and antagonists for treatment of sympathetically maintained pain
INVENTOR(S): Campbell, James N.

PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9214453	A1	19920903	WO 1992-US1543	19920226
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
EP 573581	A1	19931215	EP 1992-907852	19920226
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
JP 06507392	T	19940825	JP 1992-5073	19920226
CA 2104873	C	20000523	CA 1992-2104873	19920226
US 5447947	A	19950905	US 1992-905496	19920625
US 6559186	B1	20030506	US 1994-286404	19940805

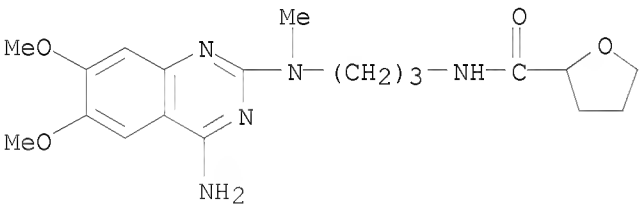
PRIORITY APPLN. INFO.:
US 1991-661554 A 19910226
US 1991-747635 A 19910820
US 1990-485156 A2 19900226
WO 1992-US1543 W 19920226

OTHER SOURCE(S): MARPAT 118:823

AB Sympathetically maintained pain (SMP) is treated topically by administering an α-1-adrenergic antagonist, α-2-adrenergic agonist, or other drug that depletes or blocks synthesis of sympathetic norepinephrine, i.e., sympatholytic agents. Examples are given showing that topical application of clonidine reduced mech. and cold hyperalgesia at the site of drug administration in patients with SMP.

IT 81403-80-7, Alfuzosin
RL: BIOL (Biological study)
(sympathetically maintained pain treatment by topical administration of)

RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



L5 ANSWER 107 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1992:644963 CAPLUS
DOCUMENT NUMBER: 117:244963
ORIGINAL REFERENCE NO.: 117:42163a,42166a
TITLE: Pharmacokinetics of alfuzosin after single oral administration to healthy volunteers, of three different doses
AUTHOR(S): Salva, P.; Bianchetti, G.; Morselli, P.; Garcia-Teresa, G.; Costa, J.
CORPORATE SOURCE: Serv. Farmacol. Clin., Hosp. Univ. Germans Trias i Pujol, Badalona, 08916, Spain

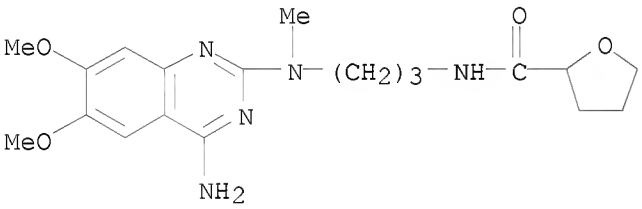
SOURCE: Biopharmaceutics & Drug Disposition (1992), 13(8), 583-90
CODEN: BDDID8; ISSN: 0142-2782
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The aim of this study was to assess the linearity of pharmacokinetics of alfuzosin, administered by oral route, at doses of 1, 2.5, and 5 mg to 12 young healthy volunteers. The pharmacokinetic parameters (tma3x, Cma3x, AUC, t1/2β) obtained from plasma alfuzosin concns. after administration of the three doses show that pharmacokinetics of alfuzosin is linear in the range of doses 1-5 mg. Mean pharmacokinetics parameters of alfuzosin observed after 1, 2.5, and 5 mg were, resp.: tmax (h) 1.5, 1.1, 1.3; Cma3x (ng mL-1) 2.6, 9.4, 13.15; AUC (ng mL-1 h) 17.7, 51.7, 99.0; t1/2 (h) 3.7, 3.9, 3.8. Cmax (Corrected by the dose) obtained after 2.5 mg was significantly higher than those obtained after 1 and 5 mg. This difference seems to be due principally to the intraindividual variability. The absence of statistically significant difference on individual values of AUC corrected by the administered dose, supports the linearity of the pharmacokinetics of alfuzosin in the range of doses between 1 and 5 mg. Some postural hypotension, clin. criterion, was observed with a frequency increasing with the dose in these healthy subjects: 0 volunteers of 12 after 1 mg, 3 volunteers of 12 after 2.5 mg and 4 volunteers of 12 after 5 mg.

IT 81403-80-7, Alfuzosin
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pharmacokinetics of, in men)

RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



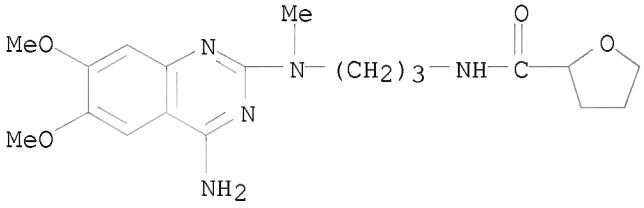
L5 ANSWER 108 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1992:248027 CAPLUS
DOCUMENT NUMBER: 116:248027
ORIGINAL REFERENCE NO.: 116:41827a,41830a
TITLE: Comparison of selective alpha-1 blockades for alpha-receptors in human hypertrophied prostatic adenomas
AUTHOR(S): Morita, Takashi; Kondo, Shun
CORPORATE SOURCE: Sch. Med., Tokyo Med. Dent. Univ., Tokyo, Japan
SOURCE: Nippon Hinyokika Gakkai Zasshi (1992), 83(3), 334-7
CODEN: NGKZA6; ISSN: 0021-5287
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB The adrenergic alpha-1 and -2 adrenoceptors in six human hypertrophied prostatic adenomas were measured in the saturation experiment using 3H-prazosin and
3H-yohimbine. Not only alpha-1 adrenoceptors but also alpha-2 adrenoceptors were found to exist in large amts. in prostatic adenomas.

In the inhibition experiment selective alpha-1 antagonists inhibited the 3H-prozosin or 3H-yohimbine binding to adenomas. The potency of alpha-1 antagonists in the order prazosin > bunazosin > alfuzosin > urapidil > terazosin and that of alpha-2 antagonists is urapidil > alfuzosin > terazosin > bunazosin > prazosin. These data suggest that urapidil, alfuzosin and terazosin may affect the human hypertrophied prostatic adenoma like phenoxybenzamine, nonselective alpha-1 antagonist, which was used for benign prostatic hypertrophy.

IT 81403-80-7, Alfuzosin
RL: BIOL (Biological study)
(prostatic adenomas of humans response to, α-adrenergic receptor blockade in relation to)

RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



L5 ANSWER 109 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN

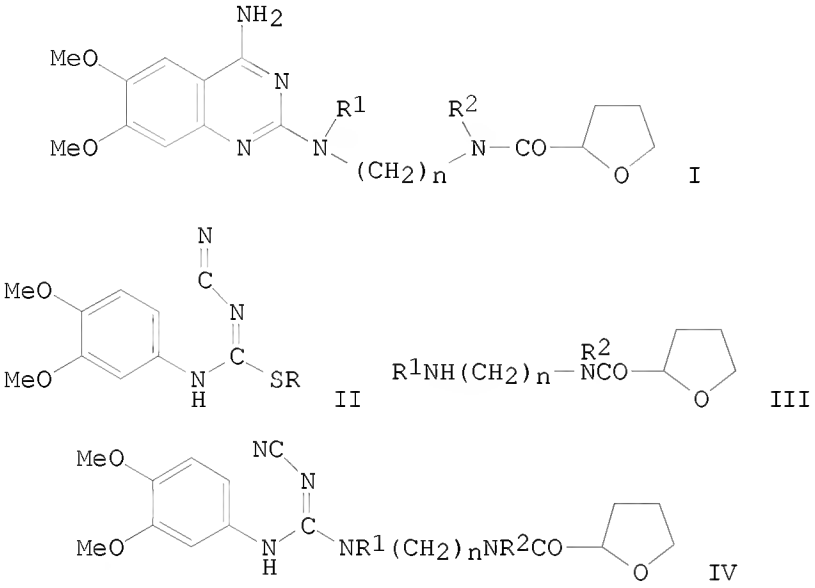
ACCESSION NUMBER: 1991:429365 CAPLUS
DOCUMENT NUMBER: 115:29365
ORIGINAL REFERENCE NO.: 115:5173a,5176a
TITLE: Preparation of quinazoline derivatives as antihypertensives
INVENTOR(S): Reiter, Jozsef; Pongo, Laszlo; Gorgenyi, Frigyes; Fekete, Marton; Csoergoe, Margit
PATENT ASSIGNEE(S): EGIS Gyogyszergyar, Hung.
SOURCE: Brit. UK Pat. Appl., 21 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2231571	A	19901121	GB 1990-8941	19900420
GB 2231571	B	19920916		
HU 53896	A2	19901228	HU 1989-1930	19890421
HU 203333	B	19910729		
HU 53903	A2	19901228	HU 1989-1931	19890421
HU 203342	B	19910729		
CA 2015066	A1	19901021	CA 1990-2015066	19900420
CA 2028953	A1	19901022	CA 1990-2028953	19900420
DK 9000990	A	19901022	DK 1990-990	19900420
SE 9001402	A	19901022	SE 1990-1402	19900420
JP 02292282	A	19901203	JP 1990-103239	19900420
ES 2019826	A6	19910701	ES 1990-1130	19900420
DD 297971	A5	19920130	DD 1990-339958	19900420
CH 681300	A5	19930226	CH 1990-1348	19900420
SU 1838309	A3	19930830	SU 1990-4743794	19900420

AT 9000931	A	19940115	AT 1990-931		19900420
PL 162976	B1	19940131	PL 1990-284860		19900420
PRIORITY APPLN. INFO.:			HU 1989-1930	A	19890421
			HU 1989-1931	A	19890421

OTHER SOURCE(S): MARPAT 115:29365

GI

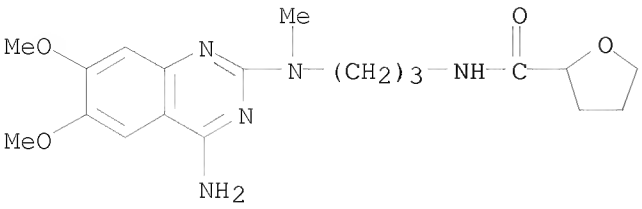


AB The title compds. [I; R1, R2 = H, alkyl, or R1R2 = (CH2)n; n = 2, 3] and their pharmaceutically acceptable salts, having α1 receptor blocking activity and therefore useful as antihypertensives (no data), were prepared by reaction of isothioureas II [R = alkyl, phenylalkyl, etc.] with amines III or by cyclization of guanidines IV. II [R = Me] was refluxed with N-(tetrahydro-2-furoyl)piperazine in isopropanol to give 92% IV [R1R2 = (CH2)2, n = 2], which in EtOCH2CH2OEt was heated at 180° for .5 h to give 73.5% I [R1R2 = (CH2)2, n = 2].

IT 81403-68-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as antihypertensive)

RN 81403-68-1 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro-, hydrochloride (1:1) (CA INDEX NAME)

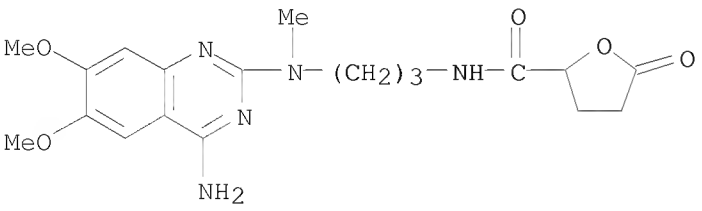


● HCl

L5 ANSWER 110 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1991:135429 CAPLUS
DOCUMENT NUMBER: 114:135429
ORIGINAL REFERENCE NO.: 114:22777a,22780a
TITLE: Design of a continuous-flow fast atom bombardment probe for a Nermag R10-10C mass spectrometer
AUTHOR(S): Vajta, S.; Padovani, P.; Gillet, G.; Thenot, J. P.
CORPORATE SOURCE: Dep. Clin. Res., Synthelabo Rech., Meudon-La-Foret, 92360, Fr.
SOURCE: Analytica Chimica Acta (1990), 241(2), 209-17
CODEN: ACACAM; ISSN: 0003-2670
DOCUMENT TYPE: Journal
LANGUAGE: English

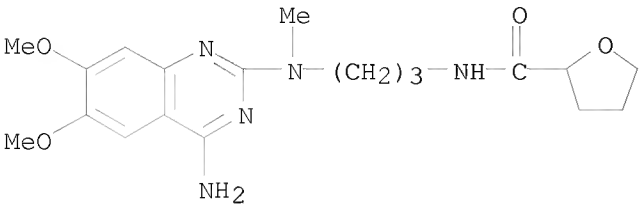
AB A probe for continuous-flow fast atom bombardment (FAB) was designed to fit a Nermag R10-10C mass spectrometer. It is made of a 1 m + 0.050 mm i.d. fused-silica capillary inserted through a 0.3 mm i.d. hole drilled axially in the copper FAB target. The pumping capacity of the mass spectrometer limited the flow-rate to 3-8 μL/min. FAB mass spectra of drugs and metabolites were obtained with a glycerol-water-methanol mixture (5 μL/min). Examples including an underivatized pentapeptide, a glycine conjugate, an N-hydroxymethyl metabolite and the differentiation between a γ-hydroxy acid and the corresponding lactone are presented.

IT 101986-74-7, Alfuzosin lactone
RL: ANT (Analyte); ANST (Analytical study)
(determination of, as alfuzosin metabolite, by fast atom bombardment mass spectroscopy)
RN 101986-74-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro-5-oxo- (CA INDEX NAME)



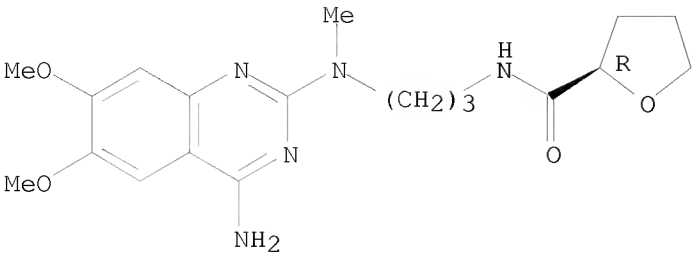
IT 81403-80-7, Alfuzosin
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(metabolism of, determination of, by fast atom mass spectroscopy)

RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



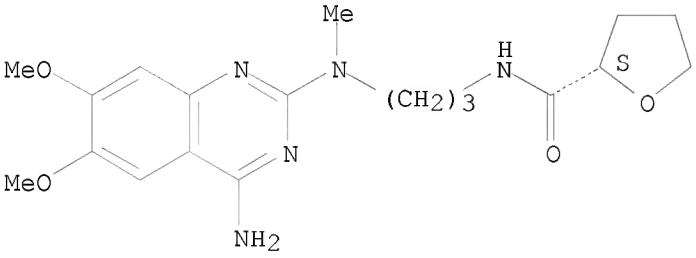
L5 ANSWER 111 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1990:470589 CAPLUS
DOCUMENT NUMBER: 113:70589
ORIGINAL REFERENCE NO.: 113:11717a,11720a
TITLE: Direct high-performance liquid chromatographic determination of the enantiomers of alfuzosin in plasma on a second-generation α1-acid glycoprotein chiral stationary phase
AUTHOR(S): Rouchouse, Alain; Manoha, Martine; Durand, Alain; Thenot, Jean Paul
CORPORATE SOURCE: Synthelabo Rech., LERS, Paris, 75013, Fr.
SOURCE: Journal of Chromatography (1990), 506, 601-10
CODEN: JOCRAM; ISSN: 0021-9673
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A direct liquid chromatog. method was developed for the determination of the enantiomers of alfuzosin in human plasma, without derivatization, on a chiral α1-acid glycoprotein column. The influence of pH, of uncharged organic solvents and of a cationic modifier (tetrabutylammonium) of the mobile phase on retention and enantioselectivity was evaluated. The enantiomers and an internal standard, structurally related to alfuzoxin, were extracted from plasma with dichloromethane-diethyl ether from alkaline solution, then
separated with a mobile phase of 0.025 M phosphate buffer (pH 7.4) containing 0.025 M tetrabutylammonium bromide-acetonitrile (94:6). The limit of quantification for each isomer was 1 ng/mL. The method has been applied to the determination of the pharmacokinetic profile of alfuzosin enantiomers in healthy volunteers after i.v. administration of the racemate.
IT 123739-69-5 123739-70-8
RL: BIOL (Biological study)
(determination in blood of humans by HPLC and pharmacokinetics of)
RN 123739-69-5 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

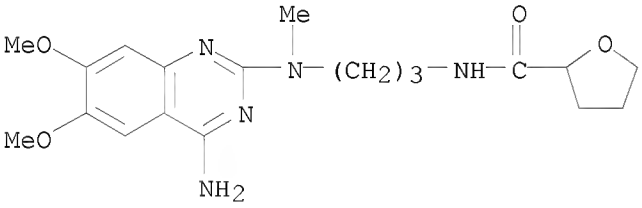


RN 123739-70-8 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 81403-80-7
RL: BIOL (Biological study)
(pharmacokinetics of enantiomers of, in humans, HPLC in determination of)
RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



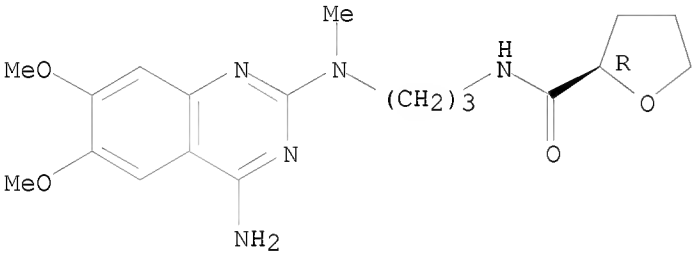
L5 ANSWER 112 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1989:624715 CAPLUS
DOCUMENT NUMBER: 111:224715
ORIGINAL REFERENCE NO.: 111:37105a,37108a
TITLE: Improved performance of the second generation α1-AGP columns: applications to the routine assay of plasma levels of alfuzosin hydrochloride
AUTHOR(S): Krstulovic, A. M.; Vende, J. L.
CORPORATE SOURCE: Synthelabo Rech., Meudon la Foret, 92366, Fr.
SOURCE: Chirality (1989), 1(3), 243-5
CODEN: CHRLEP; ISSN: 0899-0042
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Described is a direct enantioselective separation of the enantiomers of alfuzosin-HCl on the 2nd generation α1-acid glycoprotein (α1-AGP) HPLC column which offers improved efficiency, shorter anal. and improved stability with respect to the 1st generation columns. The method was applied to the anal. of the drug in rat plasma. This highly efficient extraction method and the use of fluorimetric detection resulted in selective and sensitive determination of the enantiomers. The anal. validation parameters demonstrate the applicability of this method to pharmacokinetic and metabolic studies.

IT 123739-69-5 123739-70-8
RL: ANT (Analyte); ANST (Analytical study)
(determination of, by HPLC with α1-acid glycoprotein columns)

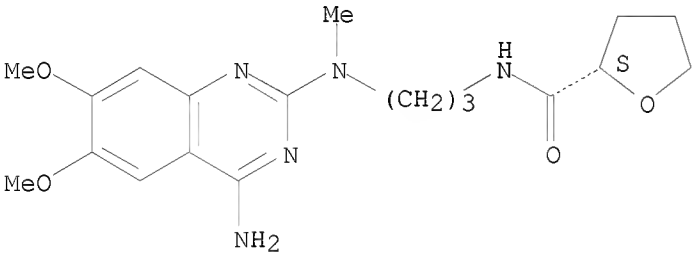
RN 123739-69-5 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



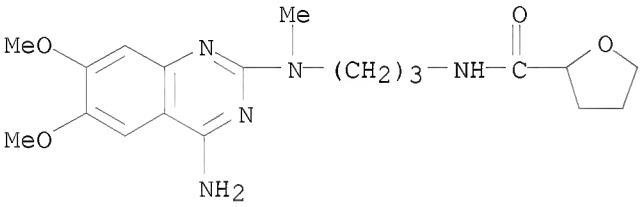
RN 123739-70-8 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 113 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1989:526433 CAPLUS
DOCUMENT NUMBER: 111:126433
ORIGINAL REFERENCE NO.: 111:20966h,20967a
TITLE: Hemodynamic and pharmacokinetic evaluation of alfuzosin in man. A dose ranging study and comparison with prazosin
AUTHOR(S): Scott, M. G.; Deering, A. H.; McMahon, M. T.; Harron, D. W. G.; Shanks, R. G.
CORPORATE SOURCE: Dep. Ther. Pharmacol., Queen's Univ., Belfast, BT9 7BL, UK
SOURCE: European Journal of Clinical Pharmacology (1989), 37(1), 53-8

CODEN: EJCPAS; ISSN: 0031-6970
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Alfuzosin, an α1-adrenoceptor antagonist, was given orally to healthy men at doses of 1, 2.5, 5, and 10 mg. Supine systolic blood (SBP) pressure was not reduced by alfuzosin although increases occurred in supine heart rate (HR) after 2.5 and 5 mg. In the standing position, SBP was reduced at 2 and 4 h with 5 mg alfuzosin; increases in HR occurred following 1, 2.5, and 5 mg at 2, 4, 6, and 8 h after administration. Exercise SBP was not reduced; diastolic blood pressure was reduced at 4 and 6 h with 5 mg alfuzosin. More marked effects were seen after 10 mg alfuzosin. After 1 and 5 mg, tmax ranged 1-2 h. The values of Cmax (4.1-20.8 ng/mL) and AUC (20-132 ng.h/mL) increased progressively with the dose, indicating dose-dependent kinetics. No changes occurred in the visual analog scale for sedation. A comparison of alfuzosin 5 mg and prazosin 1 mg administered for 4 days indicated that alfuzosin did not reduce standing SBP on either Day 1 or Day 4; prazosin reduced SBP at 2 and 4 h on Day 1 and 6 h on Day 4 compared to placebo. Standing HR was increased by alfuzosin at 2 h on Day 1 and Day 4; increases occurred with prazosin at 2, 4, 6, and 8 h on Day 1 and 6 h on Day 4. Supine plasma noradrenaline increased with alfuzosin and prazosin at 2 and 4 h on Days 1 and 4. The plasma elimination half-life (t1/2) for alfuzosin was 3.4 and 3.1 h after acute and chronic administration; t1/2 for prazosin was 2.6 and 2.9 h. Thus alfuzosin causes small redns. in systolic blood pressure accompanied by a dose-dependent increase in heart rate in the supine and standing position and following exercise.
IT 81403-80-7, Alfuzosin
RL: PRP (Properties)
(pharmacokinetics and cardiovascular effects of, in humans)
RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



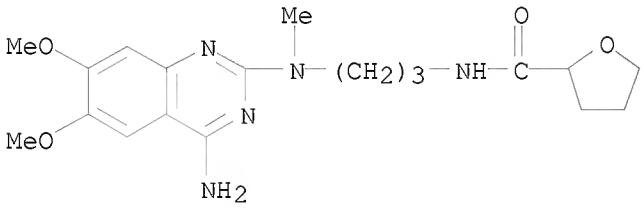
L5 ANSWER 114 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1989:88306 CAPLUS
DOCUMENT NUMBER: 110:88306
ORIGINAL REFERENCE NO.: 110:14433a,14436a
TITLE: Alfuzosin and the venous reflex response: studies in normal subjects
AUTHOR(S): Sinclair, A. J.; Davies, I. B.; Warrington, S. J.
CORPORATE SOURCE: Dep. Clin. Pharmacol., St. Bartholomew's Hosp., London, EC1A 7BE, UK
SOURCE: British Journal of Clinical Pharmacology (1989), 27(1), 19-22
CODEN: BCPHBM; ISSN: 0306-5251
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Alfuzosin is a post-synaptic α-adrenoceptor antagonist with antihypertensive and peripheral vasodilator properties. The effect of

alfuzosin, 5 mg, on sympathetically-mediated venoconstriction was measured by changes in the venous reflex response (VRR) in healthy volunteers. There was a significant inhibition of the VRR after alfuzosin compared with placebo which was present 1 h after the dose and still evident at 6 h. Supine blood pressure was lower and supine heart rate was higher after alfuzosin compared with placebo. Inhibition of the VRR by alfuzosin was observed to precede the development of reflex tachycardia.

IT 81403-80-7, Alfuzosin
RL: BIOL (Biological study)
(vein reflex response to, in humans)

RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



L5 ANSWER 115 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1989:44736 CAPLUS

DOCUMENT NUMBER: 110:44736

ORIGINAL REFERENCE NO.: 110:7327a,7330a

TITLE: Hair growth agents containing alkylenediaminoquinazolines derivatives

INVENTOR(S): Grollier, Jean Francois

PATENT ASSIGNEE(S): Oreal S. A., Fr.

SOURCE: Brit. UK Pat. Appl., 22 pp.
CODEN: BAXXDU

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

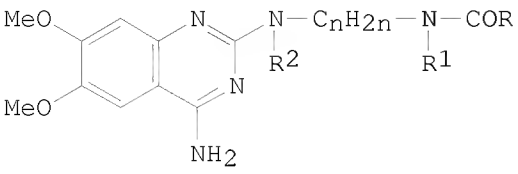
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2197589	A	19880525	GB 1987-27113	19871119
GB 2197589	B	19910123		
FR 2606635	A1	19880520	FR 1987-15952	19871118
FR 2606635	B1	19910614		
JP 63135316	A	19880607	JP 1987-289651	19871118
ES 2009222	A6	19890916	ES 1987-3289	19871118
NL 8702772	A	19880616	NL 1987-2772	19871119
DE 3739207	A1	19880728	DE 1987-3739207	19871119
BE 1000621	A3	19890221	BE 1987-1315	19871119
CH 672423	A5	19891130	CH 1987-4508	19871119
CA 1297411	C	19920317	CA 1987-552191	19871119

PRIORITY APPLN. INFO.: LU 1986-86672 A 19861119

OTHER SOURCE(S): MARPAT 110:44736

GI



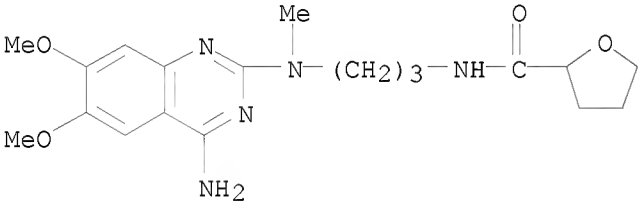
I

AB Agents to stimulate hair growth or to delay hair loss contain a diaminoquinazoline derivative [I; R = C3-6-cycloalkyl, cyclic ether residue, (dihydro)benzofuryl, cyclic sulfoxide residue; R1, R2 = H, C1-4-alkyl, PhCH2; n = 2-4]. I may have an effect on the biol. mechanisms of the pilary cycle during hair growth. A hair-growth lotion contained I-HCl (R = tetrahydrofuryl, R1 = H, R2 = Me, n = 3) 0.3, 13-cis-retinoic acid 0.025, EtOH 95, and propylene glycol to 100 g.

IT 81403-68-1
RL: BIOL (Biological study)
(hair-growth agents containing)

RN 81403-68-1 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

L5 ANSWER 116 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1988:216081 CAPLUS

DOCUMENT NUMBER: 108:216081

ORIGINAL REFERENCE NO.: 108:35331a,35334a

TITLE: Effect of acute and chronic oral administration of alfuzosin on baroreflex function and tremor in man

AUTHOR(S): Deering, A. H.; Riddell, J. G.; Harron, D. W. G.; Shanks, R. G.

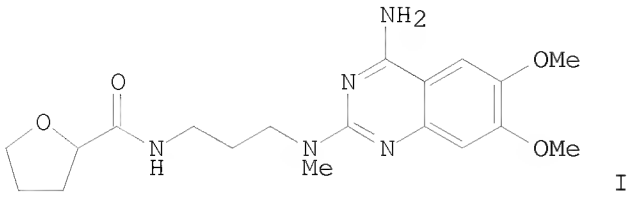
CORPORATE SOURCE: Dep. Ther. Pharmacol., Queen's Univ., Belfast, BT9 7BL, UK

SOURCE: British Journal of Clinical Pharmacology (1988), 25(4), 417-24
CODEN: BCPHBM; ISSN: 0306-5251

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



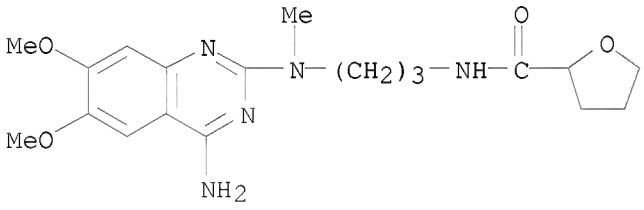
I

AB The effects of the acute and chronic administration of the α1-adrenoceptor antagonist alfuzosin(I)(5 mg twice daily, orally for 7 days) on baroreflex function, physiol. tremor and sedation (visual analog scale) were investigated in healthy human volunteers. Phenylephrine-systolic pressure dose-response curves were shifted to the right by I compared with placebo on day 1, and on day 8 prior to the administration of I indicating α-adrenoceptor blockade over 24 h with 5 mg twice daily administration. Baroreflex sensitivity (εR-R ms mmHg-1 systolic arterial pressure) was reduced by I compared with placebo on day 1 (13.8 vs. 20.6 ms mmHg-1) and on day 8 (13.4 vs 21.1 ms mmHg-1). Maximum power (μV2) or frequency (Hz) of physiol. tremor did not change 2 h after I administration on day 1 (13.7 μV2, 9.2 Hz) or day 8 (11.5 μV2, 10.0 Hz) compared with placebo on day 1 (16.9 μV2, 10.0 Hz) and day 8 (17.3 μV2, 10.2 Hz). I, 5 mg twice daily did not cause sedation on day 1 or day 8. The reduction in baroreflex sensitivity with the α-adrenoceptor antagonist I may contribute to its antihypertensive activity in reducing the reflex tachycardia associated with its hypotensive action.

IT 81403-80-7, Alfuzosin
RL: BIOL (Biological study)
(baroreflex function and tremor response to and sedation from, in humans, antihypertensive mechanism in relation to)

RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



L5 ANSWER 117 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1987:90213 CAPLUS

DOCUMENT NUMBER: 106:90213

ORIGINAL REFERENCE NO.: 106:14707a

TITLE: Alfuzosin formulations in the treatment of urinary disorders

INVENTOR(S): Regnier, Francois

PATENT ASSIGNEE(S): Synthelabo S. A., Fr.

SOURCE: Eur. Pat. Appl., 4 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 204597	A2	19861210	EP 1986-401001	19860512
EP 204597	A3	19890816		
EP 204597	B1	19920108		
R: BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
FR 2582513	A1	19861205	FR 1985-7950	19850528
FR 2582513	B1	19880805		
DK 8602465	A	19861129	DK 1986-2465	19860527
DK 168029	B1	19940124		
AU 8657951	A	19861204	AU 1986-57951	19860527
AU 586684	B2	19890720		
JP 61277620	A	19861208	JP 1986-123220	19860527
JP 05064930	B	19930916		
ZA 8603957	A	19870128	ZA 1986-3957	19860527
US 4661491	A	19870428	US 1986-867031	19860527
HU 46221	A2	19881028	HU 1986-2227	19860527
CA 1261755	A1	19890926	CA 1986-510060	19860527
IL 78934	A	19910131	IL 1986-78934	19860527

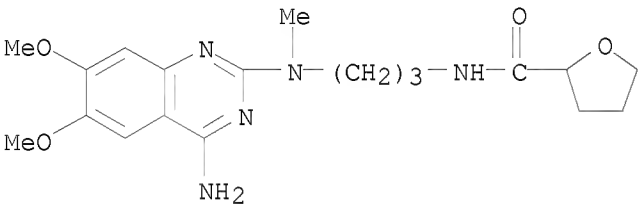
PRIORITY APPLN. INFO.: FR 1985-7950 A 19850528

AB Alfuzosin (I) injection solution contained I as the HCl 1, NaCl 44.9 mg, and water for injectio to 5 mL. Thus, as shown by sphincterometric measurements, a single i.v. injection of 5 mg I decreased by 44% the pressure at the neck of the urinary bladder in patients with neurol. dysuria.

IT 81403-80-7, Alfuzosin
RL: BIOL (Biological study)
(for treatment of urination disturbances)

RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



L5 ANSWER 118 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1986:618664 CAPLUS
DOCUMENT NUMBER: 105:218664
ORIGINAL REFERENCE NO.: 105:35115a,35118a
TITLE: A comparison of the effects of doxazosin and alfuzosin with those of urapidil on preganglionic sympathetic nerve activity in anesthetized cats
AUTHOR(S): Ramage, Andrew G.
CORPORATE SOURCE: Acad. Dep. Pharmacol., R. Free Hosp. Med. Sch., Hampstead/London, NW3 2PF, UK
SOURCE: European Journal of Pharmacology (1986), 129(3), 307-14
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal

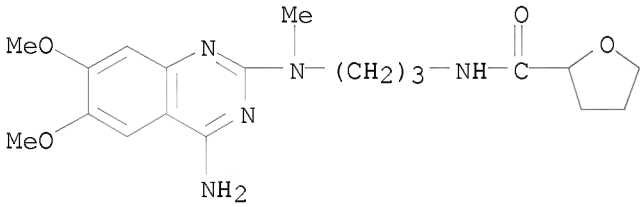
LANGUAGE: English

AB Preganglionic sympathetic nerve activity, blood pressure, heart rate, and femoral arterial conductance were recorded in anesthetized, paralyzed cats. Urapidil [34661-75-1], doxazosin mesylate [77883-43-3], and alfuzosin [81403-80-7] were infused i.v. for 1 h into different animals at the rate of 2 mg/kg/h. All three drugs caused a fall in thoracic preganglionic sympathetic nerve activity along with blood pressure. Although urapidil had a greater hypotensive action than doxazosin and alfuzosin its sympathoinhibitory action was delayed and weaker. Since all three drugs are α1-adrenoceptor antagonists it appears that antagonism at this receptor type may cause central sympathoinhibition as well as a decrease in total peripheral resistance. However, the different effects of urapidil suggest that its action on central sympathetic tone and therefore its hypotensive action cannot be due entirely to its ability to block α1-adrenoceptors.

IT 81403-80-7
RL: BIOL (Biological study)
(antihypertensive activity of and preganglionic sympathetic nerve activity decrease by, α1-adrenoceptor blockade in relation to)

RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



L5 ANSWER 119 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1986:527471 CAPLUS

DOCUMENT NUMBER: 105:127471

ORIGINAL REFERENCE NO.: 105:20427a

TITLE: Synergistic antihypertensive

INVENTOR(S): Cavero, Icilio; Hicks, Peter; Langer, Salomon

PATENT ASSIGNEE(S): Synthelabo S. A. , Fr.

SOURCE: Fr. Demande, 5 pp.
CODEN: FRXXBL

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2570275	A1	19860321	FR 1984-14088	19840914
FR 2570275	B1	19861121		
JP 61072718	A	19860414	JP 1985-4810	19850114
JP 05037407	B	19930603		
EP 178961	A1	19860423	EP 1985-401730	19850906
EP 178961	B1	19900808		
R: BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
IL 76377	A	19891215	IL 1985-76377	19850912
DK 8504161	A	19860315	DK 1985-4161	19850913
DK 160034	B	19910121		

DK 160034	C	19910617		
AU 8547430	A	19860424	AU 1985-47430	19850913
AU 574506	B2	19880707		
ZA 8507057	A	19860625	ZA 1985-7057	19850913
HU 40569	A2	19870128	HU 1985-3463	19850913
HU 193448	B	19871028		
CA 1256031	A1	19890620	CA 1985-490635	19850913

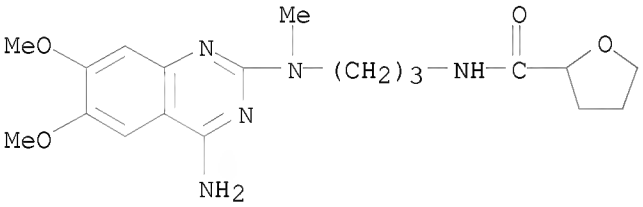
PRIORITY APPLN. INFO.: FR 1984-14088 A 19840914

AB A composition containing 30-160 mg diltiazem and 0.1-10 mg alfuzosin is a synergistic antihypertensive. Thus, spontaneously hypertensive rats were infused i.v. with diltiazem (10 μg/kg/min) for 45 min, and 10 min later alfuzosin (2 μg/kg/min) for 5 min. The decrease in blood pressure by the drug combination was much more marked than that shown by the drugs alone.

IT 81403-80-7
RL: BIOL (Biological study)
(antihypertensive drug containing diltiazem and, synergistic)

RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



L5 ANSWER 120 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1986:527470 CAPLUS

DOCUMENT NUMBER: 105:127470

ORIGINAL REFERENCE NO.: 105:20427a

TITLE: Pharmaceutical compositions containing an α-blocker and a calcium antagonist

INVENTOR(S): Cavero, Icilio; Cazor, Jean Louis; Hicks, Peter; Langer, Salomon

PATENT ASSIGNEE(S): Synthelabo S. A. , Fr.

SOURCE: Eur. Pat. Appl., 14 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 189336	A1	19860730	EP 1986-400015	19860107
R: BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
FR 2576214	A1	19860725	FR 1985-678	19850118
FR 2576214	B1	19870220		
FR 2577803	A1	19860829	FR 1985-2725	19850226
FR 2577803	B1	19870403		
FR 2577804	A1	19860829	FR 1985-2726	19850226
FR 2577804	B1	19870327		
DK 8600223	A	19860719	DK 1986-223	19860117
AU 8652456	A	19860724	AU 1986-52456	19860117

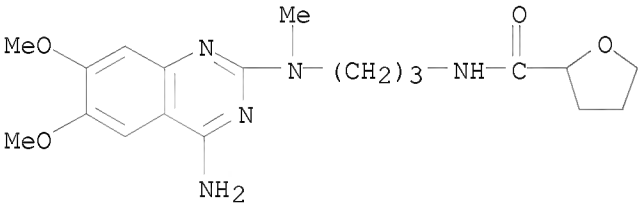
JP 61167626	A	19860729	JP 1986-8820		19860117
HU 39604	A2	19861029	HU 1986-243		19860117
ZA 8600379	A	19861029	ZA 1986-379		19860117
US 4925837	A	19900515	US 1987-106968		19871013
PRIORITY APPLN. INFO.:			FR 1985-678	A	19850118
			FR 1985-2725	A	19850226
			FR 1985-2726	A	19850226
			US 1985-692767	B2	19850116
			US 1986-817262	B1	19860109
			US 1986-846032	B1	19860331

AB Compns. containing α-blocking agents, such as alfuzosin, prazosin, terazosin, etc. and a Ca2+ antagonist, such as diltiazem, nifedipine, and verapamil, are synergistic antihypertensives. Thus, oral administration of 0.3 mg prazosin + 12.5 mg diltiazem/kg very markedly decreased the systolic pressure in spontaneously hypertensive rats, whereas the components by themselves were much less effective.

IT 81403-80-7
RL: BIOL (Biological study)
(antihypertensive agent containing calcium antagonist and, synergistic)

RN 81403-80-7 CAPLUS

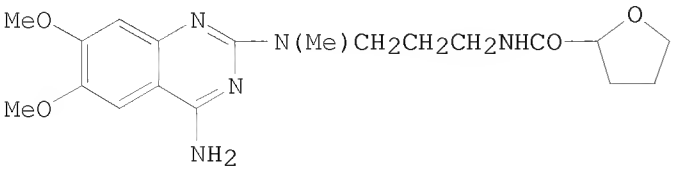
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



L5 ANSWER 121 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER:	1986:179613 CAPLUS
DOCUMENT NUMBER:	104:179613
ORIGINAL REFERENCE NO.:	104:28261a,28264a
TITLE:	High-performance liquid chromatographic determination of alfuzosin in biological fluids with fluorometric detection and large-volume injection
AUTHOR(S):	Guinebault, P.; Broquaire, M.; Colafranceschi, C.; Thenot, J. P.
CORPORATE SOURCE:	Lab. Etud. Rech. Synthelabo, Dep. Clin. Res., Meudon-La-Foret, 92360, Fr.
SOURCE:	Journal of Chromatography (1986), 353, 361-9 CODEN: JOCRAM; ISSN: 0021-9673
DOCUMENT TYPE:	Journal
LANGUAGE:	English

GI



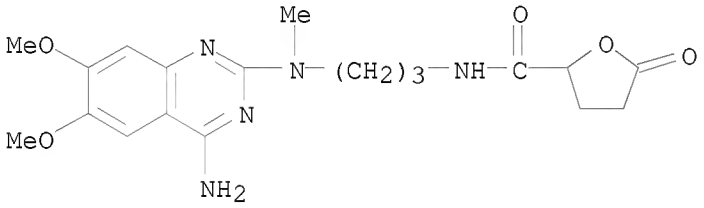
I

AB An HPLC method for the determination of alfuzosin (I) [81403-80-7], a new antagonist of α1 postsynaptic adrenergic receptors, in blood, plasma, or urine is described. With fluorometric detection and the large-volume injection technique, the limit of detection in plasma is 0.5-1 ng/mL, which is sensitive enough for pharmacokinetic studies in man. The calibration graph is linear between 1 and 200 ng/mL in blood plasma, with coeffs. of variation of 6.2% and 1%, resp. In urine, the linearity range is 0.05-10 μg/mL; at the lowest concentration, the coefficient of variation is .apprx.10%. A constant plasma-to-blood concentration ratio (1.25) allows the measurement of drug in either fluid. In blood or plasma, I is stable at 37° for 24 h and at -20° for 6 mo. As expected for reversed-phase chromatog., the retention times of I and a few of its analogs decrease inversely with the concentration of MeCN in the mobile phase. However, as this concentration reaches about 75%, the retention times increase sharply; this may be explained by interactions of the amino groups with silanol groups of the stationary phase.

IT 101986-74-7
RL: BIOL (Biological study)
(HPLC of, mobile phase effects in)

RN 101986-74-7 CAPLUS

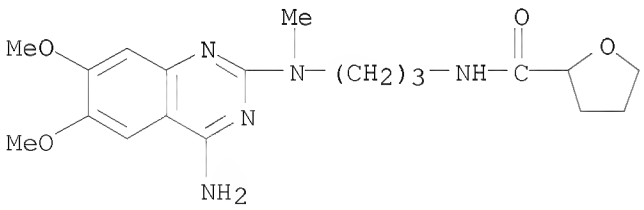
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro-5-oxo- (CA INDEX NAME)



IT 81403-80-7
RL: ANT (Analyte); ANST (Analytical study)
(determination of, in blood and urine of humans by HPLC with fluorometric detection and large-volume injection)

RN 81403-80-7 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



L5 ANSWER 122 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1986:148830 CAPLUS

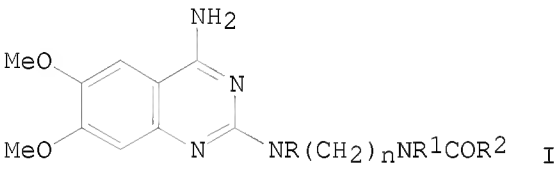
DOCUMENT NUMBER: 104:148830

ORIGINAL REFERENCE NO.: 104:23561a,23564a

TITLE: Synthesis and antihypertensive activity of a series of 4-amino-6,7-dimethoxyquinazoline derivatives

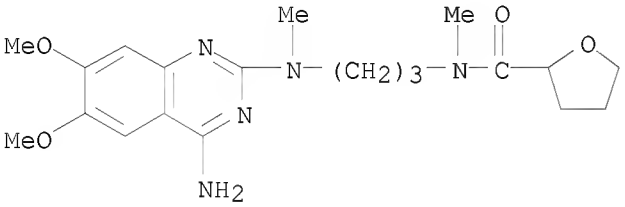
AUTHOR(S): Manoury, Philippe M.; Binet, Jean L.; Dumas, Andre P.;

Lefevre-Borg, Francoise; Cavero, Icilio
CORPORATE SOURCE: Chem. Dep., Lab. Etud. Rech. Synthelabo, Bagneux, 92220, Fr.
SOURCE: Journal of Medicinal Chemistry (1986), 29(1), 19-25
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 104:148830
GI

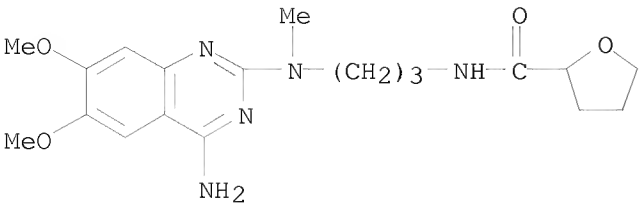


I

AB N2-[(Acylamino)alkyl]-6,7-dimethoxy-2,4-quinazolinediamines I (e.g., R, R1, R2, n = Me, Me, Ph, 2; Me, H, tetrahydro-2-furyl, 3) were synthesized as potential α1-adrenoceptor antagonists. In rats at 10 mg/kg po, some I (n = 3) showed good antihypertensive activity, whereas I (n = 2) did not.
IT 76362-33-9P 81403-68-1P 81403-73-8P
81403-80-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antihypertensive activity of)
RN 76362-33-9 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro-N-methyl- (CA INDEX NAME)

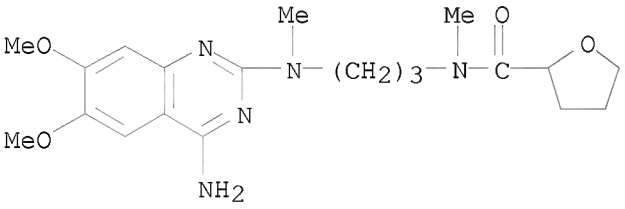


RN 81403-68-1 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro-, hydrochloride (1:1) (CA INDEX NAME)



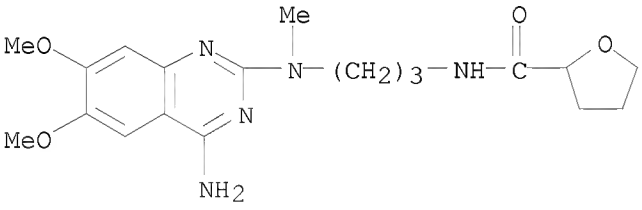
● HCl

RN 81403-73-8 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro-N-methyl-, monohydrochloride (9CI) (CA INDEX NAME)



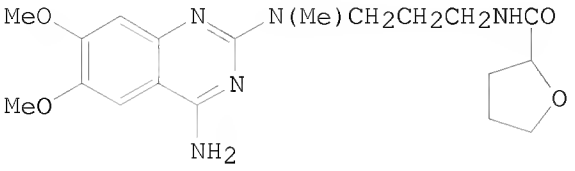
● HCl

RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



L5 ANSWER 123 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1985:214546 CAPLUS
DOCUMENT NUMBER: 102:214546
ORIGINAL REFERENCE NO.: 102:33491a,33494a
TITLE: Absolute bioavailability of alfuzosin, a new α1-post synaptic receptor antagonist, after oral and intravenous administration
AUTHOR(S): Guinebault, P.; Colafranceschi, C.; Bianchetti, G.; Thenot, J. P.; Maillard, D.; Thiercelin, J. F.; Larribaud, J.; Morselli, P. L.
CORPORATE SOURCE: LERS-Synthelabo, Paris, 75013, Fr.
SOURCE: Biopharm. Pharmacokinet., Eur. Congr., 2nd (1984),

Volume 2, 578-83. Editor(s): Aiache, J. M.; Hirtz, J. Lavoisier: Paris, Fr.
CODEN: 53JFAA
DOCUMENT TYPE: Conference
LANGUAGE: English
GI



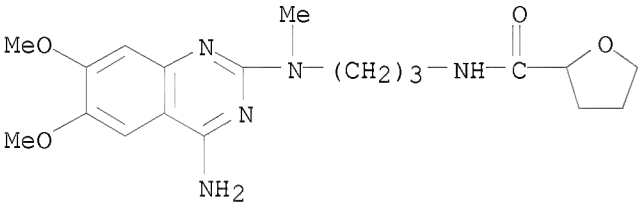
I

AB The pharmacokinetics and absolute bioavailability of alfuzosine (I) [81403-68-1] was studied in healthy volunteers after i.v. or oral administration of I at 5 mg. The pharmacokinetic profile of I after i.v. administration was identical to that found after oral administration. The results indicated that 64% of the oral dose of I was available for the systemic circulation. I pharmacokinetics was linear with 5-40 mg doses.

IT 81403-68-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bioavailability and pharmacokinetics of, after i.v. or oral administration in human)

RN 81403-68-1 CAPLUS

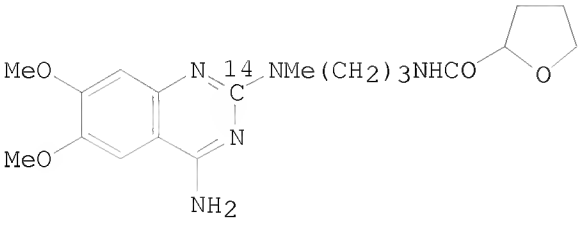
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

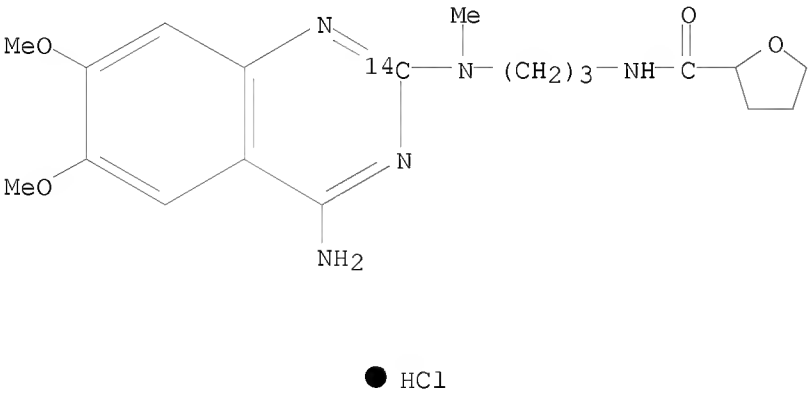
L5 ANSWER 124 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1984:209735 CAPLUS
DOCUMENT NUMBER: 100:209735
ORIGINAL REFERENCE NO.: 100:31847a,31850a
TITLE: A synthesis of alfuzosine-14C hydrochloride
AUTHOR(S): Allen, J.
CORPORATE SOURCE: Dep. Chem., Synthelabo - LERS, Bagneux, 92220, Fr.
SOURCE: Journal of Labelled Compounds and Radiopharmaceuticals (1983), 20(11), 1283-6
CODEN: JLCRD4; ISSN: 0362-4803
DOCUMENT TYPE: Journal

LANGUAGE: English
OTHER SOURCE(S): CASREACT 100:209735
GI



I

AB The title compound (I.HCl) was prepared from K14CNO by sequential cyclization with 2,4,5-H2N(MeO)2C6H2CO2H, chlorination, amination, and condensation with N-[(3-methylamino)propyl]tetrahydrofuran-2-carboxamide.
IT 89563-97-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 89563-97-3 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl-2-14C)methylamino]propyl]tetrahydro-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

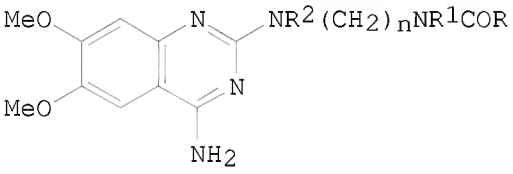
L5 ANSWER 125 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1982:162737 CAPLUS
DOCUMENT NUMBER: 96:162737
ORIGINAL REFERENCE NO.: 96:26795a,26798a
TITLE: 4-Amino-6,7-dimethoxyquinazolin-2-ylalkylenediamines
INVENTOR(S): Manoury, Philippe M.
PATENT ASSIGNEE(S): Synthelabo S. A. , Fr.
SOURCE: U.S., 6 pp. Cont.-in-part of U.S. Ser. No. 8,931, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4315007	A	19820209	US 1979-99622	19791210
FR 2421888	A1	19791102	FR 1978-3175	19780206
FR 2421888	B1	19800926		
FR 2445323	A2	19800725	FR 1978-36819	19781229
FR 2445323	B2	19811127		
ZA 7900455	A	19801029	ZA 1979-455	19790202

PRIORITY APPLN. INFO.: FR 1978-3175 A 19780206; FR 1978-36819 A 19781229; US 1979-8931 A2 19790202

OTHER SOURCE(S): MARPAT 96:162737

GI



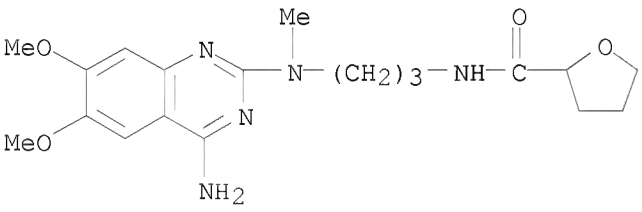
I

AB Antihypertensive (no data) quinazolinyl alkylenediamines I (R = cycloalkyl, oxacycloalkyl, thiacycloalkyl, benzofuryl; R1, R2 = H, alkyl, CH2Ph; n = 2-4) were prepared Thus, tetrahydrofuroic acid was treated with MeNHCH2CH2CN followed by reduction of the cyano group and treatment with 4-amino-2-chloro-6,7-dimethoxyquinazoline to give I (R = 2-tetrahydrofuryl, R1 = H, R2 = Me, n = 3).

IT 81403-68-1P 81403-73-8P 81403-80-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 81403-68-1 CAPLUS

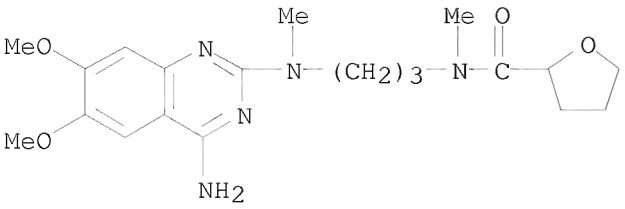
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

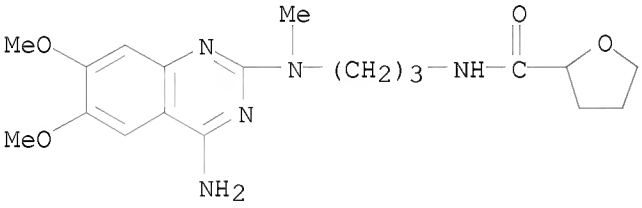
RN 81403-73-8 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro-N-methyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

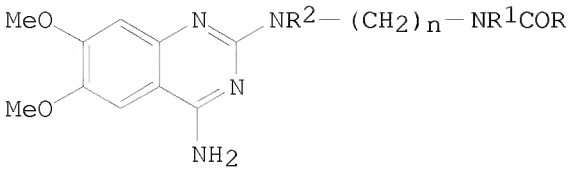
RN 81403-80-7 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro- (CA INDEX NAME)



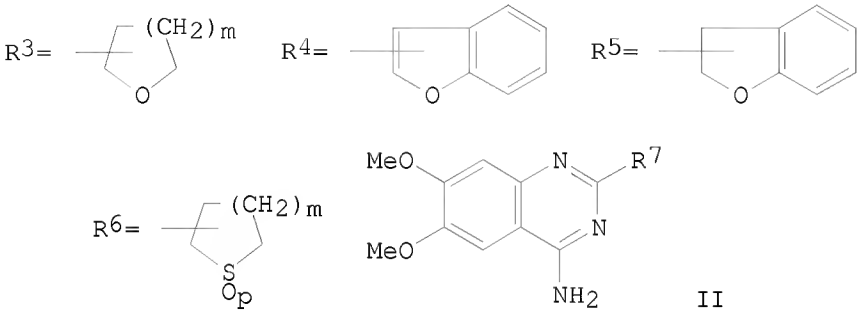
L5 ANSWER 126 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1981:65722 CAPLUS
DOCUMENT NUMBER: 94:65722
ORIGINAL REFERENCE NO.: 94:10721a,10724a
TITLE: Alkylenediamine derivatives
INVENTOR(S): Manoury, Philippe
PATENT ASSIGNEE(S): Synthelabo S. A., Fr.
SOURCE: Belg., 16 pp. Addn. to Belg. 873,909.
CODEN: BEXXAL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
BE 879730	A4	19800430	BE 1979-197895		19791030
FR 2466462	A2	19810410	FR 1979-24373		19791001
FR 2466462	B2	19830114			
DE 3004554	A1	19810402	DE 1980-3004554		19800207
PRIORITY APPLN. INFO.:			BE 1979-873909	A	19790202
			FR 1979-24373	A	19791001

OTHER SOURCE(S): CASREACT 94:65722; MARPAT 94:65722
GI



I



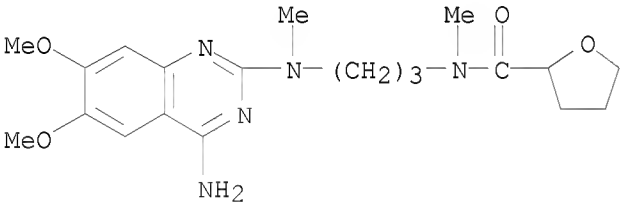
II

AB The antihypertensive (no data) alkylenediamines I [R = C3-6 cycloalkyl, R3 (m = 0, 1, 2)), R4, R5, R6 (m , p = 0, 1, 2); R1, R2 = H, C1-4 alkyl, PhCH2; n = 2, 3, 4] were prepared by condensation of quinazoline II (R7 = halo) and R2NH(CH2)nCN followed by reduction and acylation. Thus, mixed anhydride condensation reaction of tetrahydro-2-furoic acid with MeNHCH2CH2CN followed by hydrogenation over Rh-Al2O3 gave R8CONMe(CH2)3NH2 (R8 = tetrahydro-2-furyl) (III). III condensed with II (R7 = Cl) to give I (R = tetrahydro-2-furyl, R1 = Me, R2 = H, n = 3), isolated as HCl salt.

IT 76362-33-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 76362-33-9 CAPLUS

CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro-N-methyl- (CA INDEX NAME)



L5 ANSWER 127 OF 127 CAPLUS COPYRIGHT 2008 ACS on STN

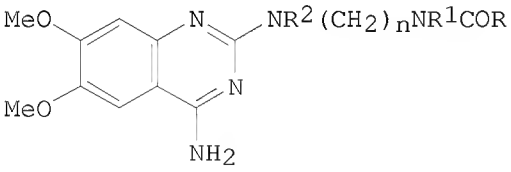
ACCESSION NUMBER: 1980:6552 CAPLUS
DOCUMENT NUMBER: 92:6552
ORIGINAL REFERENCE NO.: 92:1235a,1238a
TITLE: Alkylenediamine derivatives
INVENTOR(S): Manoury, Philippe Michel Jacques
PATENT ASSIGNEE(S): Synthelabo S. A., Fr.
SOURCE: Ger. Offen., 14 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2904445	A1	19790816	DE 1979-2904445	19790206
DE 2904445	C2	19861030		
FR 2421888	A1	19791102	FR 1978-3175	19780206
FR 2421888	B1	19800926		
FR 2445323	A2	19800725	FR 1978-36819	19781229
FR 2445323	B2	19811127		
BE 873909	A1	19790802	BE 1979-193248	19790202
DK 7900460	A	19790807	DK 1979-460	19790202
DK 159316	B	19901001		
DK 159316	C	19910304		
AU 7943895	A	19790816	AU 1979-43895	19790202
AU 521524	B2	19820408		
ZA 7900455	A	19801029	ZA 1979-455	19790202
IL 56578	A	19830223	IL 1979-56578	19790202
FI 7900369	A	19790807	FI 1979-369	19790205
FI 66861	B	19840831		
FI 66861	C	19841210		
NO 7900358	A	19790807	NO 1979-358	19790205
NO 151463	B	19850102		
NO 151463	C	19850417		
SE 7900987	A	19790807	SE 1979-987	19790205
SE 449360	B	19870427		
SE 449360	C	19870806		
AT 7900842	A	19810515	AT 1979-842	19790205
AT 365176	B	19811228		
CA 1102330	A1	19810602	CA 1979-320864	19790205
CH 637122	A5	19830715	CH 1979-1120	19790205
JP 60023114	B	19850605	JP 1979-12737	19790205
NL 7900917	A	19790808	NL 1979-917	19790206
NL 181482	B	19870401		
NL 181482	C	19870901		
GB 2013679	A	19790815	GB 1979-4032	19790206
GB 2013679	B	19820902		

PRIORITY APPLN. INFO.: FR 1978-3175 A 19780206
FR 1978-36819 A 19781229

GI



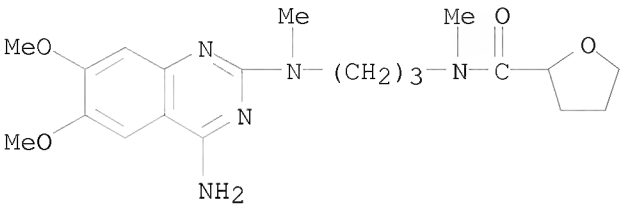
I

II

AB Quinazolylalkylenediamines I (R = cycloalkyl, O- or S-containing heterocycle; R1, R2 = H, C1-4 alkyl, CH2Ph; n = 2-4) were prepared Thus, 2-tetrahydrofurancarboxylic acid was treated with MeNHCH2CH2CN to give II (R3 = CN) which was reduced to II (R3 = CH2NH2) followed by treatment with 4-amino-2-chloro-6,7-dimethoxyquinazoline to give I (R = 2-tetrahydrofuryl, R1 = Me, R2 = H, n = 3). At 10 mL/kg orally, I caused .apprx.35% decrease in systalic blood pressure of spontaneously hyptertensive rats 2 h after administration.

IT 72104-36-0P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 72104-36-0 CAPLUS
CN 2-Furancarboxamide, N-[3-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]propyl]tetrahydro-N-methyl-, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

=> d his

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FILE 'REGISTRY' ENTERED AT 10:55:26 ON 06 OCT 2008
L1 STRUCTURE UPLOADED
L2 6 S L1
L3 86 S L1 FULL

FILE 'CAPLUS' ENTERED AT 10:56:34 ON 06 OCT 2008
L4 360 S L3
L5 127 S L4 NOT PY>2003

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	XXXXXXXXXXXXXXXX	

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-101.60	-101.60

STN INTERNATIONAL LOGOFF AT 10:58:02 ON 06 OCT 2008